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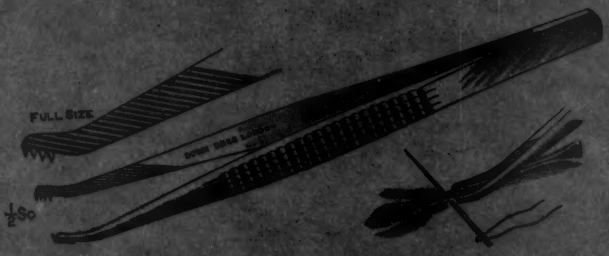

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VOL. 42, No. 1 NEW SERIES FEBRUARY, 1935

The Treatment of Prolapse

BY

A. LEYLAND ROBINSON, M.D. (Lond.), F.R.C.S. (Eng.), F.C.O.G.

Professor of Midwifery and Gynaecology, University of Liverpool; Hon. Surgeon, The Hospital for Women, Liverpool; Hon. Surgeon, The Maternity Hospital, Liverpool.

IF treatment is to be rational rather than empirical, it must be founded upon the aetiology and pathology of the disease in question, and, therefore, it is only proper that any discussion upon the treatment of prolapse should be preceded by a short survey of the causation of this condition.

CAUSATION.

Congenital predisposition. Congenital defect is probably more common than is generally supposed to be the case, for in addition to the association that exists between so-called congenital prolapse and *spina bifida*, this influence is shown by the occasional appearance of severe prolapse in nulliparae and the rapid onset of prolapse in some young primiparae after normal labour. Moreover, every surgeon has noted marked variations in the development of the perineal and pelvic muscles of different patients, and has experienced from time to time great difficulty in finding good muscular tissue in the course of plastic operations upon the pelvic floor.

Acquired lesions. The efficiency of the musculature supporting the birth canal may be impaired in two ways, namely, by lacerations which produce mechanical defects, and by muscular

weakness or atrophy induced by subinvolution, the menopause, or severe debility.

In the causation of prolapse, subinvolution and frank injuries generally act in liaison with each other, but of the two, subinvolution is the more important factor. A severe injury sustained during labour can hardly be overlooked, nor can it fail to receive immediate and generally adequate attention, but loss of muscle tone may supervene after a perfectly natural delivery in which there is no injury whatever, or it may be associated with hidden injuries, such as internal rupture of the levator ani muscles, or splitting of the fibres of the paracolpos, pubocervical and uterosacral ligaments. In the presence of such unsuspected damage, impairment of tone of the pelvic muscles is apt to be overlooked and the condition of weakness to pass unnoticed until the onset of symptoms draws the attention of the patient to the existence of prolapse.

Activating Causes.

Any factor which increases the abdominal pressure, such as constipation, overwork, or bronchitis, for instance, is competent to initiate descent in a woman who is predisposed towards this complaint by congenital or acquired weakness.

Principles of Treatment.

Prevention. Any procedure that protects the pelvic muscles from undue pressure, over-stretching or laceration, will tend to prevent descent of the uterus and vagina by preserving the integrity of the supports of the birth canal. The preventive treatment of prolapse is, therefore, dependent upon good antenatal work, skilful midwifery and careful puerperal supervision.

The value of a sound and uninjured pelvic floor should always be taken into account when the respective merits of delivery *per vias naturales* and delivery by Caesarean section are under consideration. In many cases in which the indications for laparotomy are not absolute, it should be remembered that the peritoneal adhesions and other sequelae of a Caesarean section may amount to less disability than the traumata that are likely to be inflicted upon the pelvic floor by the forcible delivery of the child's head through the maternal passages.

I should also like to emphasize the value of episiotomy for the prevention of prolapse. Unaided delivery in which the mother is not injured is properly considered to be the ideal in

midwifery, but when this end can only be achieved by long waiting, there may be great over-stretching of the pelvic muscles and much harmful interference with their vascular supply.

In these circumstances there may be no obvious injury, but I am convinced that prolonged pressure reduces the nutrition and sometimes destroys the tone of the supporting muscles and that excessive conservatism may be responsible for the development of prolapse. A well-judged episiotomy designed to cut short this harmful period of waiting and dangerous pressure is, in my opinion, a prophylactic measure of real value and one that ought to be employed more frequently.

The Use of Pessaries.

Pessaries are useful for three purposes: (1) Diagnosis. (2) As a temporary measure for healthy women in the childbearing period. (3) As a palliative measure for women in whom operation is unduly hazardous on account of age or bodily weakness.

Surgical Treatment.

Operation. Surgical intervention is indicated during the reproductive period for the repair of injuries that weaken the pelvic supports and for the relief of symptoms that cannot be controlled by other means, but I regard operation as absolutely curative only when reproduction has ceased, for I do not believe that any surgeon can hope to improve upon nature or to guarantee freedom from recurrence in the event of future childbearing.

Technique.

I agree with Victor Bonney that the surgeon must employ an anatomical method of repair and that he must judge each case on its own merits with due regard to the type of injury and the functional requirements of the patient.

There are two main clinical groups, and these may be further subdivided into minor types which depend upon the anatomical situation of the principal lesion: (1) Simple vaginal prolapse, including cystocele, rectocele, or both, in which the middle and upper supports are intact and the lower ones at fault. (2) Uterovaginal prolapse, of which there are two kinds, one in which the descent is chiefly uterine and the other chiefly vaginal; here the main injury or weakness is centred in the middle supports.

It seems to me impossible to conceive of uterine apart from

vaginal prolapse, because if the uterus drops at all, it is bound to invert at least the upper part of the vagina.

In my submission, all the supports of the birth canal and uterus may be approached from the vagina with the exception of the round ligaments, but I look upon the latter as the least important elements of the supporting apparatus and consider their help to be but rarely required for the cure of ordinary prolapse.

The normal function of the round ligaments is to check excessive backward movements of the uterus, and by maintaining anteflexion, to protect this organ from the full force of intra-abdominal pressure, but I cannot believe that they ordinarily play any direct part in maintaining the level of the pelvic organs. They are never taut under natural conditions, and although they must come into action when descent begins, their supporting power is feeble and ill adapted to resist the further descent of the uterus. These ligaments may reinforce the other supports of the uterus, but they can never replace them successfully, and it is, therefore, impossible to cure genital prolapse by means of abdominal operations alone.

For these reasons, and chiefly because I am convinced that the main supports are all readily accessible from below, I am a firm believer in the efficacy of vaginal operations for the cure of prolapse, and I am confident that the practised operator will rarely find it necessary to enlist the aid of the round ligaments or adventitious fixation bands. At the same time, even the most perfervid believer in vaginal work must admit that laparotomy is sometimes a desirable and indeed a necessary addition.

There are, I think, three groups of cases which come into this category: (1) Severe types of prolapse in nulliparae: experience has shown that recurrence is not infrequent in such cases, unless the effects of congenital hypoplasia are treated by radical measures. (2) Severe and growing prolapse in young women during the active reproductive period in which pessaries are for some reason contra-indicated: the additional support afforded by the round ligaments or a ventralfixation band will enable the surgeon to reduce the severity of minor operation and to limit the sacrifice of vaginal tissue. (3) Patients suffering from complicated prolapse, when there are retroversion, prolapsed ovaries or pelvic infection: these and other complications cannot be treated via the vaginal route and, therefore, it is essential that the abdomen should be opened in such cases.

The experience derived from my own series of approximately 1,000 operations has convinced me of the soundness underlying

the technique which was initiated in St. Mary's Hospital, Manchester, over 40 years ago by Professor Donald, and subsequently modified by the late Dr. Fothergill.

With the so-called "Manchester operation", all operators are familiar, and I propose to confine myself to three steps in the technique which are in my opinion of some importance.

1. *Incision of the Anterior Vaginal Wall.*

In connexion with the cure of cystocele, I should like to draw attention to a simple but effective way of treating urethral prolapse and stress incontinence by means of a slight modification of the ordinary method of performing anterior colporrhaphy.

Most operators begin their incision into the anterior vaginal wall from a point above the urethral orifice and run upwards and backwards towards the lateral fornix on each side.

I begin my incision from two points which are picked up outside the urethra on each side. I then join these two points by a slightly curved incision which runs across the vagina above the urethral orifice, and then complete the rest of the incision in the usual way. This technique paves the way for the excision of the bulge which is generally such a conspicuous feature near the urethral orifice and enables the operator to construct a grid for the support of the urethra and the relief of stress incontinence.

The upper vaginal stitches are inserted from side to side, sometimes in mattress fashion, but in the lower part I modify this arrangement by placing my deep stitches laterally and my superficial sutures antero-posteriorly, thus producing a T-shaped grid scar in the anterior vaginal wall near the urethral opening which gives a pleasing aesthetic appearance and a good functional result. This manœuvre may be said to put a reef into the triangular ligament and the pubo-cervical muscle of Bonney.

2. *Cervical Repair.*

I aim at restoring the uterus to its normal length by excising the redundant portion of the enlarged cervix and pay special attention to the reconstruction of the external os, because the technique employed for this purpose affords an opportunity for dealing with the slackened parametric tissue that is now exposed to view.

The surgical importance of the structure as a whole is now well recognized, but I do not think that the true significance of the utero-sacral elements has yet been appreciated. It is a striking fact that during vaginal or abdominal hysterectomy the

uterus is more readily and more completely mobilized by division of the utero-sacral ligaments than by the division of any other part of the parametrium.

If this be true, then the converse must hold good, namely that the uterus can be more readily and more completely immobilized by tightening up the relaxed utero-sacral ligaments than by the repair of any other part of the parametrium.

I believe that elongation of the utero-sacral ligaments resulting from lacerations, or subinvolution, leads to slackness of the whole of the parametric tissue, and causes not only descent but retroversion of the uterus, and that when the utero-sacral ligaments are made taut again they tighten up and correct both prolapse and retroversion.

Blair-Bell, in an address some years ago, described a method of achieving this object by stitching the utero-sacral ligaments together through an abdominal incision, but I am of the opinion that the same result may be obtained through the vaginal route if special care is taken to insert the cervico-vaginal stitches in a particular manner.

The utero-sacral ligaments are accessible (and visible) in the postero-lateral fornix when the mucous membrane of the vagina has been divided at a distance from the cervix, and their muscular matrix is readily picked up by a needle passed outwards and backwards in the direction of the sacrum.

When these sutures are tied, the shortened ligaments pull the cervix upwards and backwards and restore the uterus to its normal level and position.

This method has an advantage over the more usual procedure of placing deep stitches in the cardinal ligaments lying at the sides of the cervix, because in the utero-sacral region there is no likelihood of encountering the ureter or of injuring large vessels.

3. *Peritoneal Incision.*

Many textbooks in describing the perineal incision, direct the operator to pick up points on the posterior edge of the nymphae and to use these points as a guide to the margin of the perineal incision. If this be carried out, the new perineum will join the vulva at an acute angle and the original curve of the vestibule will be replaced by a sharp edge. Moreover, this technique does not make any provision for the reconstruction of the vulva, and unless great care is exercised it is liable to cause atresia of the vaginal orifice and to be followed by severe dyspareunia.

I think these disadvantages may be avoided by carrying out

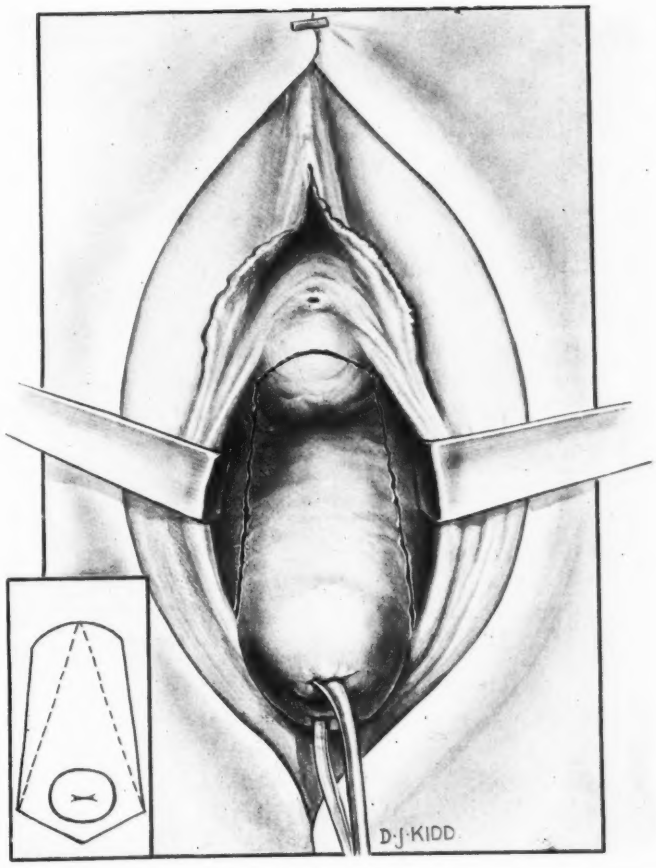

FIG. 1. Modification of ordinary incision (inset) for cure of cystocele.

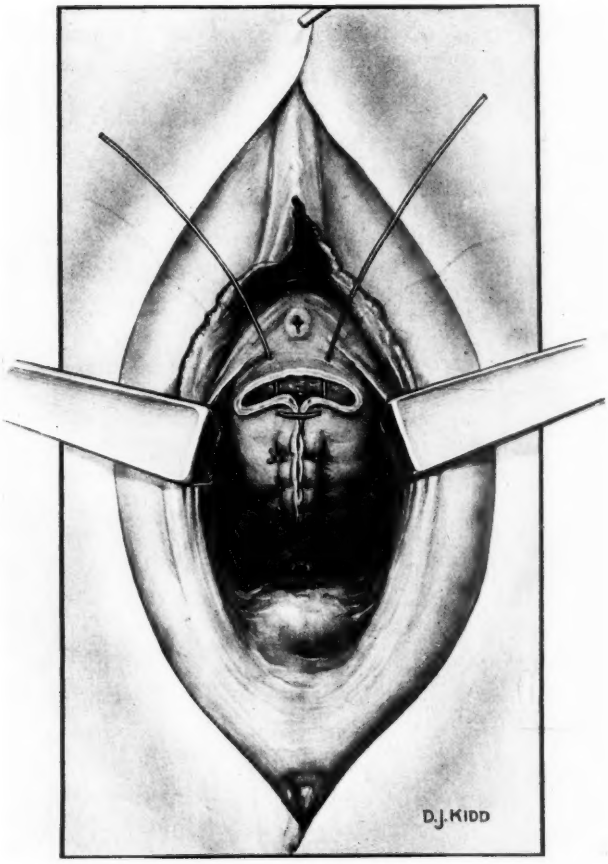

FIG. 2. Completion of anterior colporrhaphy showing excision of urethral bulge and resulting T-shaped scar.

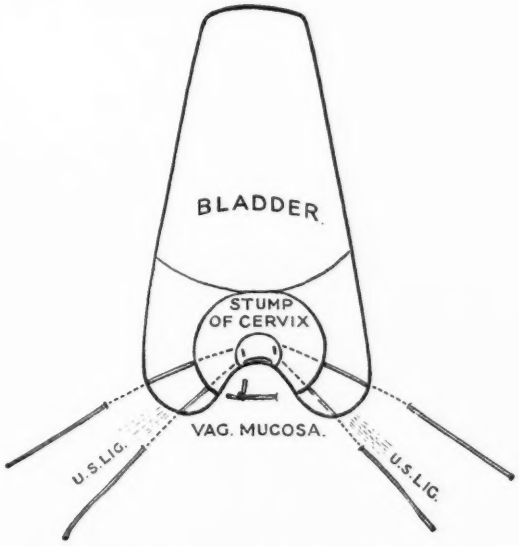

FIG. 3. Diagram to represent method of inserting stitches into the utero-vesical ligaments during the reconstruction of the cervix and os uteri.

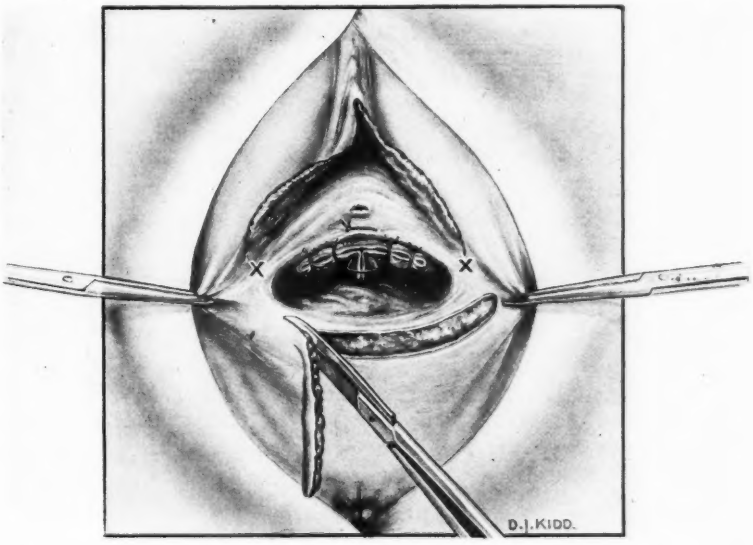

FIG. 4. Modification of ordinary incision for perineorrhaphy. Compare the area picked up by the Kocher's forceps on each side with the points (represented by an x) which are generally adopted as the anterior limits of the incision.

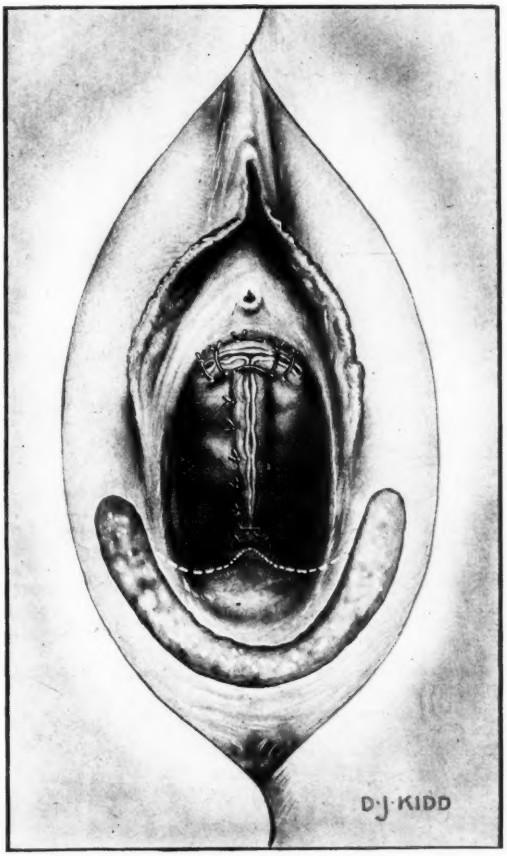

FIG. 5. Perineal incision completed and that for posterior colporrhaphy indicated by white dotted lines. Note the final result of the anterior colporrhaphy operation.

the original incision in a different manner. An oval area (not a point) is chosen on the outer side of the nympha on each side and a portion of tissue corresponding to the displaced *labium majus* is chosen in accordance with the age, parity and functional requirements of the patient, but it is essential that the antero-lateral margin of the incision should always be placed on the outer side of the posterior boundary of the nympha.

By using this method, the reconstruction of the perineal body is greatly facilitated, all sharp angles are abolished, and atresia of the vulval outlet is rendered impossible: a further advantage is to be derived from the fact that the length of the vagina is increased rather than diminished.

The views expressed in this paper upon the operative treatment of proplapse may be summed up in three sentences:—

1. Prolapse can never be cured by an abdominal operation alone.
2. Prolapse can nearly always be cured by a vaginal operation alone.
3. The treatment of prolapse occasionally demands an abdominal as well as a vaginal operation.

The Post-natal Development of the Genital Organs in the Albino Rat

With a Discussion of a New Theory of Sexual Differentiation.

BY

B. P. Wiesner, Ph.D., D.Sc.,

Late Macaulay Lecturer, University of Edinburgh.

VI. Effects of Sex Hormones in the Heteronomous Sex

(*Continued from p.* 922, *vol.* xli, 1934.)

The Transformation of the Clitoris into a Penis-like Organ.

In these experiments proviron—the preparation of the comb-growth-promoting substance mentioned previously—was injected into a number of females aged from four to seven days. Only seven out of 34 animals survived for more than two days. The survivors were killed between the eighteenth and twenty-first day of life; they had received two or three injections of the hormonic solution. Table V shows the details of the procedure. The clitoris and ovaries were sectioned serially: specimen sections of the other organs were prepared.

In order to interpret the results it must be borne in mind that the preparation used in these experiments contained a not inappreciable amount of cornifying hormone; this explains the occurrence of cornification in one instance.

The effect upon the clitoris was very marked in three instances, and definite in two; while in two cases a detectable effect was not produced. In these last two cases the clitoris was indistinguishable from that of a normal female of equivalent age.

In the "positive" cases (particularly in animals Nos. 2 and 5) the changes produced were recognizable even by inspection with the naked eye. The urogenital papilla—i.e. the dermal sac enshrouding the clitoris—was greatly enlarged and exceeded in size that of the intact litter-brothers. Pressure upon the papillae produced the escape of thin strands of yellow secretion from the ducts of the glandulae clitoridis. The quantity of this secretion

TABLE V.

Designation	Animal No.	Age	Age at first injection	Age at second injection	Age at third injection	Quantities of hormone administered: Proviron	Quantities of hormone administered: Keto-hydroxy-oestrin	Weight of ovaries	State of vagina	Maximum diameter of clitoris	Maximum diameter of cartilage: Dorso-ventral	Maximum diameter of cartilage: Trans-versal	Papillae: Maximum height	Papillae: Number
		days	days	days	days	mgm.	mgm.	mgm.		mm.	mm.	mm.	μ	
Proviron experiment ...	1	21	4	9	13	7	—	3·8	op.	1·65	·75	·3	32	72
	2	18	4	9	16	9	—	4·2	cl.	1·85	·75	·3	28	62
	3	18	4	9	13	9	—	4·7	cl.	1·8	·6	·4	30	88
	4	18	4	11	13	9	—	4·0	op.*	1·6	·65	·4	34	46
	5	21	5	11	—	18	—	5·1	cl.	2·2	1·05	·35	40	74
	6	21	4	9	13	9	—	4·5	cl.	1·45	—	—	—	—
	7	21	5	7	12	9	—	5·6	cl.	1·4	—	—	18	12
Controls ...	8	18	—	—	—	—	—	5·6	cl.	1·45	—	—	—	—
	9	21	—	—	—	—	—	4·8	cl.	1·2	—	—	—	—
	10	21	—	—	—	—	—	5·2	cl.	1·4	—	—	—	—
	11	21	4	9	13	—	—	5·7	cl.	1·35	—	—	—	—
	12	21	4	9	13	—	—	6·0	cl.	1·45	—	—	—	—
Proviron-Ketohydroxy-oestrin experiment	13	21	4	8	14	7	·08	4·8	op.	1·45	—	—	20	31
	14	21	4	8	14	7	·08	4·3	op.	1·8	·55	·4	32	62
	15	21	4	8	14	7	·2	4·9	op.	1·6	·65	·4	30	48
	16	21	4	8	14	7	·1	5·1	cl.	1·9	·9	·4	36	51
Means: Proviron ...	—	—	—	—	—	10	—	4·5	—	1·77	·76	·38	30·3	59
Means: Controls ...	—	—	—	—	—	—	—	5·4	—	1·33	—	—	—	—
Means: Proviron-oestrin ...	—	—	—	—	—	7	·11	4·8	—	1·69	·52	·3	29·5	48

op.—open cl.—closed *—cornified

Measurements of the clitoris ("maximum diameter") are represented by the values $\left(2\sqrt{\frac{A}{\pi}}\right)$ where A is the area of the largest cross-section through the glans clitoridis (planimetric measurements). This indirect method is required in view of the change in shape produced by masculinization (see Fig. 5 and 7, Plate III). The greatest diameter calculated for the clitoris of mature females is 1·75 mm.

exceeded that procurable from normal animals. Enlargement of the papilla was noticeable within two days after the first injection. Within three to seven days after the first injection macroscopic inspection revealed yet another change. Normally the opening of the dermal sac in the female is almost round and very narrow; the clitoris lies deeply within the sac and pressure upon the side walls of the latter does not expose the organ. In the experimental animals under discussion the orifice of the dermal sac became slit-shaped and relatively large; pressure upon the sides exposed a small glans rather similar to the glans penis of a very young male. The most striking change became obvious when this glans was inspected more closely. It was then seen that a thin cartilaginous process projected from the region immediately dorsal from the orifice of the urethra. This process was indistinguishable from the cartilaginous process of the os priapi.

Sections through the clitoris of these animals confirmed the impression that a certain measure of masculinization had been achieved. The size of the clitoris markedly exceeded that of control animals. The integument, normally smooth, indifferent and fused with the epithelial lining of the dermal sac, had undergone a measure of stratification, and in two cases no connexion with the lining of the sac existed in the apical region.* The integument resembled that of the penis of a prepuberal animal in yet another respect: it was not smooth but contained anlagen of papillae.† Their structure, size and number corresponded to those of the anlagen found in the integument of the glans penis of males aged about three to six weeks. The integument was not only more highly differentiated than that of the normal clitoris, but it was also more extensive. It has been mentioned that the epithelial folds which, by their inner leaf, form the integument of the clitoris, only cover the dorsum clitoridis—they extend to about the level of the dorsal surface of the urethra. In the experimental animals under

*This may partly be explained by the pressure exerted during examination *in vivo*; stratification itself, however, cannot be reduced to this factor since it was not observed in the clitoris of untreated animals exposed to similar examination.

† It has been shown recently that thelykinin produces epithelial changes in certain parts of the male genital tract; this effect represents a corollary to the action of androkinin upon the clitoris. On the other hand, a slight degree of stratification appears in the integument of the apex of the mature clitoris; its causation is unknown.

discussion, they extended further ventrally, but did not in any instance surround the whole glans clitoridis, whereas in the pubescent male, they envelop the glans penis.

The corpus cavernosum of the glans clitoridis also showed considerable changes. Instead of the unspecific tissue that constitutes the corpus in the intact animal, a parenchyma of the type found in prepuberal males developed. Numerous radial interstices separated by trabecles of male structure were present; blood was scanty. The great variability in the number of these cavernae in the male and the small number of surviving females makes it impossible to draw quantitative comparisons; but in two cases it would have been difficult to distinguish the parenchyma of the corpus cavernosum of the transformed clitoris from that of a male of equivalent age. While the histological structure of the corpus cavernosum clitoridis thus resembled that of the male, there were considerable differences in size. In the male the corpus, at the age of three weeks, completely surrounds the remaining structures of the glans penis. In the transformed clitoris it was more voluminous than in the specimen from intact females, but it did not surround the urethra.

The mode of development of the cartilaginous process (which constitutes a macroscopical sign of transformation) is doubtful. It seems to originate from an area of small darkly-staining cells situated in the apex of the clitoris (see p. 902, vol. 41), but by what stages the elements of the process develop is doubtful, since in five cases a complete cartilage was found, while in the remaining two negative cases not any vestige of cartilaginification was discovered; thus an indication of the initial development of the process was not available.

It is of particular interest that the changes in the clitoris of the "positive" cases were not restricted to the formation of the cartilaginous process, but extended to the development of those accessory cavernous spaces which were described as a characteristic feature of the normal glans penis. In the transformed clitoris these spaces with their trabecles and cavernae extend into the vicinity of the apex of the cartilage; they have no manifest equivalent in the clitoris of the untreated female.

The dorsal region of the spongiosa accompanying the urethra in the normal clitoris seems to undergo a certain degree of involution in the experimental animals. The spaces were less numerous in the proximal region of the urethra. On the other hand, the sub-urethral spongiose tissue showed considerable development. The epithelium of the urethra had undergone

stratification of an intensity exceeding that of the normal female urethra.

A few experiments on older animals have also been carried out; growth of the cartilage can also be induced in such animals, but only one group of animals need be referred to in this context. The commercial preparation Hombreol, stated to contain 4 cock's-comb-units per cc., was used. Seven females, aged 29 days at the first injection, received intra-peritoneal injections (0.5 cc. each) on alternate days; they were killed one week after the first injection.

The external measures of the clitoris were taken from the fresh specimen as described for the penis. In addition, the corresponding measures were taken from seven untreated litter-sisters of the experimental animals. In the latter the maximum dorso-ventral diameter of the clitoris varied from 1.45 mm. to 1.65 mm. (A.M. = 1.53 mm.). In the experimental animals the measures ranged from 1.7 mm. to 1.85 mm. (A.M. = 1.80 mm.). As in the group discussed above, differences in reaction were pronounced not only with respect to size of the glans clitoridis but also with respect to differentiation. Reference to the possible theoretical significance of differential reactivity will be made later. (See p. 58.)

There can be no doubt that the observed transformation of the clitoris was due to the conditions of the experiment and cannot be ascribed to chance incidence. The writer has had occasion to examine, during the past four years, more than 3,000 females of the same stock, bred under identical conditions; but only one case, to be described later, of "spontaneous" virilism comparable to the cases under discussion, has been observed.* On the other hand, five out of seven surviving animals which were exposed to the action of "male hormone" showed the transformation. The probability that this result was due to chance incidence is less than 1:10,000; in other words, the transformation may be referred to the action of male hormone with very great certainty.

As to the nature of the changes there can be no doubt that they represent an approximation to the male type of development

*Shortly before this case was discovered Miss A. Hain informed the writer that she had observed several cases of what she regarded as "intersexuality" in a litter of albinos derived from the writer's stock. Superficial examination by the writer indicated that these animals exhibited virilism like the case mentioned here. But this occurrence does not materially reduce the probability of masculinization being due to the action of androkinin.

of the urogenital tubercle. The presence of a cartilaginous process, the structure of the corpus cavernosum, the size of the organ, the stratification of the integument with the concomitant formation of primordial papillae, the development of accessory cavernous spaces—all these are typical characters of the penis not proper to the clitoris.

Little can be said on the basis of the available evidence concerning the action of male hormones upon the ovary and the uterus. The differentiation of the uterus is already noticeable in animals four days old; and of the newborn animals which were injected with proviron none survived the treatment. In the animals which received the first injection when at least four days old, no influence of the experimental conditions upon the development of the uterus was discovered. Indirect planimetry failed to establish significant differences and the differentiation was complete.

As to the ovaries, structural differences between the experimental and control animals respectively were not discovered.* Differences in size may have existed, but the available material is not large enough to justify any conclusion; ovarian weights, in very young females, are difficult to establish in view of the relatively large errors incurred in preparation and weighing.

Administration of Thelykinin to Newborn Males.

The corollary to the experiments described in the preceding paragraphs is represented by a series of experiments in which ketohydroxy-oestrin was injected in newborn males, varying concentrations and total amounts being administered to the experimental animals. It was found convenient to use a suspension of the hormone in aqueous alcohol. Details of three experiments are presented in Table VI; it should be understood, however, that the data relating to the quantities administered are only approximate, in some instances, since the technique in the original experiments was somewhat inadequate. Part of the injected fluid escaped from the injection canal in consequence of the very low tonus of the skin of newborn animals; this source of error was eliminated in later experiments. The total number of animals surviving the treatment was 29.

The results of these experiments were not uniform. The injection of small quantities of the hormone did not affect to any appreciable extent the development of the genital system

* The epoöphoron was highly developed in two cases.

which was examined both macroscopically and microscopically. On the other hand, medium and large quantities resulted in a definite interference with development. The most obvious effect was upon the growth of the testes and the penis. The former did not attain, in any instance, the weight of the smallest gonad found in the intact controls or of those males which had received only injections of aqueous alcohol. The size of the glans—which was ascertained by measuring, not the fresh specimen, but the cross-sections—was also very definitely below the minimum attained by the glans penis of the intact litter-brothers. The seminal vesicles were somewhat smaller than those of control animals; but the difference, though consistent, was not very marked. The vesicles were of normal shape.

Microscopically it was found that the glans penis was incompletely differentiated in all animals that had received medium or large doses of hormone preparation. The anterior process was completely absent or very small in every case but two; the corpora cavernosa showed comparatively few interstices and were formed by embryonic cells even in the animals killed at the age of three weeks. The cavernous tissue accompanying the urogenital sinus was also incompletely developed. The accessory cavernous bodies mentioned in the description of the normal penis and producible by injections of androkinin in the female, were found in all but two specimens; but they did not appear to be as well developed as in the normal male. The integument showed comparatively few primordial papillae, and had retained, over much of its surface, the smooth appearance it exhibits in the newborn and very young male. The os priapi was thinner than normally, but ossification had occurred.

The effects of the injection upon the peripheral (dependent) genital characters can be likened to the effect of castration when the latter is carried out at birth. It is not quite so drastic since the diameter of the glans penis of the injected animals exceeded in some instances that of specimens from castrates fixed and embedded in the same way. But the conclusion that the injections had an effect nearly equalling that of castration is unavoidable with respect to both growth and differentiation. As to differentiation, a distinction between effects of castration and administration of thelykinin must be made mainly with regard to the development of the corpus cavernosum which, in the injected animals, failed to degenerate into that highly unspecific tissue found in the corpora cavernosa of the castrates.

But all this holds true only for the animals which had

TABLE VI.

Nature of experiment	Number of surviving animals	Age at death	Number of injections	Amount of hormone	Maximum diameter of glans penis			Diameter of cartilage									Diameter of os priapi			Number of papillae			Maximum height of papillae	Weight of testes			Seminal vesicles	
								Dorsoventral						Transversal														
					min.	AM.	max.	min.	AM.	max.				min.	AM.	max.				mim.	AM.	max.					Length	Weight
		days		mgm.	mm.	mm.	mm.	mm.	mm.	mm.				mm.	mm.	mm.				mm.	mm.	mm.	μ	min. mm.	AM. mm.	max. mm.	AM. mm.	AM. mgm.
Injection of ketohydroxyoestrin (B.D.H.)	5	14	6	·0024	2·0	2·15	2·2	·75	·76	·8				·55	·57	·6				·22	·25	·28	77	89	103	38	42·5	51·3	57·5	—	—
	6	21	10	·02	1·25	1·27	1·35	·16	·22	·28				·16	·17	·19				·19	·22	·24	49	62	71	60	35·2	35·3	36·5	—	3·3
	5	14	8	1·44	1·2	1·55	1·85	0	·12	·32				0	·05	·12				·16	·17	·18	12	21	50	50	30·2	32·9	37·3	2·9	—*
Control injected with aqueous alcohol	2	21	9	—	2·0	2·2	2·4	·85	·85	·85				·55	·57	·6				·22	·25	·28	97	104	112	55	65·4	72·5	79·7	3·4	—
	3	14	6	—	1·9	2·0	2·3	·7	·75	·8				·55	·57	·6				·19	·28	·29	98	105	115	35	49·0	50·3	51·5	2·8	—
Castrates (uninjected)	2†	22	—	—	1·4	1·5	1·6	--	—	—				—	—	—				·2	·23	·25	42	53	65	45	—	—	—	2·3	—
	4‡	14	—	—	1·3	1·45	1·7	—	—	—				—	—	—				·18	·20	·22	60	66	68	—	—	—	—	1·9	—
Castrates injected with menformon §	7	14	5	?	1·2	1·35	1·7	—	—	—				—	—	—				·22	·24	·28	53	61	77	35	—	—	—	2·1	—

* Not determined. † R. 715-2 and R. 608-4; see Table I (page 882, vol. xli). ‡ R. 797-2, 3; R. 1172-2, 4; see Table I. § 400 units.

Measurements taken from fixed specimens.

received massive doses of ketohydroxy-oestrin; a detectable effect was not produced by the small doses.

Effect of Massed Doses of Thelykinin upon Males Castrated at Birth.

Seven males were castrated when not more than 12 hours old; they received injections of concentrated solution of a commercial preparation of crystalline thelykinin (menformon). Details are presented in Table VI (p. 15).

The experiments were undertaken in order to determine whether feminization of the glans penis could be effected by large doses of female hormone. Feminization might be represented by a suppression of the development of the os priapi which does not appear in the clitoris; the process might also involve other changes resulting in the development of an organ resembling the clitoris to a higher degree than does the glans penis of the castrate.

Yet the examination of the specimen failed to show any such effect. No difference between the preparations collected from castrates of corresponding ages and the specimens under discussion was discovered. Neither the size nor the degree of differentiation of the glans manifested any detectable influence of the administration of thelykinin.

Effect of Simultaneous Administration of Thelykinin and Androkinin.

It remains to discuss briefly the effects of simultaneous administration of thelykinin and androkinin respectively. Such experiments were undertaken both in female and in male rats and the same samples of ketohydroxy-oestrin and proviron which were utilized in the experiments previously described were also employed in the cases now under discussion. As has been mentioned before, the writer has not been successful in rearing newborn females injected with any but the smallest quantities of proviron; so that only observations on slightly older rats are available; but, as will be seen presently, this limitation is not of great importance. It should also be mentioned that the writer did not follow the example of Moore and Price[49, 50] who injected mixtures of androkinin and thelykinin which had been allowed to stand for some time before being administered; in the cases under discussion, the injections were given separately, one follow-

ing immediately upon the other, since the female hormone was used in alcoholic solution, the male in oily solution.*

Effect of Mixtures on Females.

As to females it should be emphasized that the experiments in which masculinization of the clitoris was effected by means of proviron, represent to some extent an exposure of females to mixtures of the two gonadic hormones since the sample of proviron used contained a not inappreciable quantity of cornifying hormone. It remained only to be seen, therefore, whether large quantities of thelykinin would effect what small quantities failed to do—i.e. prevent the masculinizing effect of androkinetic substance.

The experiments—details of which are presented in Table V—failed to reveal any influence even of large quantities of ketohydroxy-oestrin. It is difficult to draw any reliable quantitative comparisons since the number of animals surviving this drastic treatment was small and the variation in the degree of masculinization was wide—both in the group under discussion and in the animals receiving proviron only. But while it is impossible to prove definitely that there did not exist any quantitative difference between the two groups, this conclusion seems very likely. As to the qualitative changes produced by solutions containing large quantities of ketohydroxy-oestrin and relatively little proviron, they equalled those occurring after injections of proviron alone. The formation of a cartilaginous process, of accessory cavernous spaces and of papillae in advanced stages of differentiation as well as the transformation of the indifferent tissue constituting the corpus cavernosum glandis penis were established in higher or lesser degree in all but one case; in the latter only slight indications of masculinization (represented by the formation of orimentary papillae; freezing sections only) were found.

Thelykinin thus failed to protect the clitoris against the masculinizing influence of androkinin; conversely, the latter failed to interfere with the hysterotropic effect of the female hormone to any detectable extent. The genital tract of the experimental females showed enlargement; but the animals were killed too late after the last injection to permit significant conclusions.

*The first injection of proviron was given in these experiments on the fourth day of life.

TABLE VII.

Experiment	Number of animals	Age at death	Number of injections	Amount of hormone: Ketohydroxy-oestrin	Amount of hormone: Proviron	Diameter of glans penis: min.	Diameter of glans penis: AM.	Diameter of glans penis: max.	Diameter of cartilage: Dorsoventral min.	Dorsoventral AM.	Dorsoventral max.	Diameter of cartilage: Transversal min.	Transversal AM.	Transversal max.
		days		mgm.	mgm.	mm.	mm.	mm.	mm.	mm.	mm.	mm.	mm.	mm.
Entire injected ...	7	21	9	0·18	27	2·3	2·3	2·4	·68	·72	·75	·5	·54	·56
Castrated at birth and injected ...	5	18	7	0·14	18	1·7	1·85	1·9	·61	·63	·68	·28	·29	·34
Entire controls ...	12	21	—	—	—	2·3	2·45	2·7	·75	·76	·8	·5	·57	·58

TABLE VII. *(continued)*

Experiment	Diameter of os priapi: min.	Diameter of os priapi: AM.	Diameter of os priapi: max.	Number of papillae: min.	Number of papillae: AM.	Number of papillae: max.	Height of papillae: AM.	Weight of testes: min.	Weight of testes: AM.	Weight of testes: max.	Length of seminal vesicles: AM.
	mm.	mm.	mm.	mm.	mm.	mm.	μ	mgm.	mgm.	mgm.	mm.
Entire injected ...	·25	·26	·29	65	73	94	58	79	82	84	3·1
Castrated at birth and injected ...	·24	·25	·28	74	83	99	45	—	—	—	2·6
Entire controls ...	·22	·27	·28	81	96	112	55	116	123	134	3·0

EFFECT OF COMBINED HORMONE SOLUTIONS UPON MALES.

In the last experiment to be reviewed in this context a number of newborn males received injections of ketohydroxy-oestrin from birth onward; from the third to the fifth day onward they also received injections of proviron while the administration of the female hormone was continued. Details of procedure and results are shown in Table VII.

The effects of the injections can be briefly summarized in the statement that the animals in question could hardly be distinguished from normal animals, and were slightly better developed than castrates treated with proviron. The glans penis did not lack the anterior process, but the process was less well developed than in normal animals. The corpus cavernosum was well differentiated; papillae in advanced stages of differentiation were found and the diameter of the glans differed but slightly from that of the normal animal. The seminal vesicles were developed to the stage they normally reach at the age at which the experimental animals were killed save for a doubtful increase in the height of the epithelium. The testes, on the other hand, were smaller than normal.* Histologically they showed no distinct abnormality.

As in the experiment described in the preceding section of the present chapter, it is almost impossible to assert with complete certainty that no quantitative differences exist between the effects of the administration of proviron to castrates on one hand, of mixtures of proviron and ketohydroxy-oestrin to normal males on the other hand. A very extensive set of experiments would be required to establish the apparent identity of effects. But apart from possible minor differences, the qualitative effects are identical; in either case the inhibition of peripheral differentiation (produced either by castration or by the administration of female hormone) is neutralized by the administration of proviron; even excessive and unphysiological quantities of thelykinin failed to interfere with the activity of androkinin.

DISCUSSION.

THE SIGNIFICANCE OF THE MASCULINIZATION OF THE CLITORIS

It has already been stated that the effect of androkinin upon the clitoris must be regarded as a partial masculinization and

*However, they were actually heavier than the testes of males injected with oestrin only. This finding is of doubtful significance, since variation of testicular weight is pronounced.

cannot be regarded as a chance incidence of virilism. This result is in accordance with observations recorded by previous authors. Thus Lipschütz[51] described the peniculus formed in the female guinea-pig carrying functional testis grafts; moreover, Voss and Loewe[52] relate a similar effect in guinea-pigs injected with preparations of androkinin.

It can be assumed, with a high degree of certainty, that the females in which transformation was observed would have developed into normal animals—that is, females with a normal clitoris. Obvious considerations show that this conclusion represents only a different way of expressing that the results could not be ascribed to chance. Yet the inherent tendency towards, and potency for, female differentiation was overridden by the administration of male hormone in the majority of cases. It may be concluded that the divergent differentiation of the primordia of the clitoris and the penis respectively is not due to an inherent constitutional difference between these primordia, but to a difference in the *milieu intérieur*, characterized by the presence or absence of male hormone respectively. It appears that the conditions of male differentiation (mainly represented by the circulation of androkinin) are dominant over those of female differentiation.

The experiments thus tend to support the theorem of equipotentiality. The fact that the anlagen of both clitoris and penis react with male development to the same condition appears to indicate the existence of an "alternative Reactionsnorm." At the same time it must be conceded that the experiments are incomplete (and are, under the present conditions of research on androkinin, bound to remain so for some time to come); for it has not been shown that exactly the same quantities are needed to effect, say, the formation of an anterior process in the female and male tubercle respectively.

Equipotentiality is also indicated by another observation. It will be remembered that castration effects complete inhibition of the development of the anterior process, interferes with the differentiation of the cavernous tissue and reduces the complexity of the integument, reduces growth-rate and ultimate size of the penis, but does not prevent the ossification of the os priapi. Conversely, masculinization of the clitoris is constituted mainly by the enlargement of the organ, the differentiation of the cavernous body, the formation of a cartilaginous process and the appearance of papillae while no os is formed. In other words, those constituents of the glans penis which are affected most by

castration are most readily produced in the clitoris and vice versa. The differential reaction of the various parts of the penis to castration has been explained by differential rates in the attainment of determination. It seems probable that the same conditions prevail in the clitoris; rates of determination seem to be similar in clitoris and penis respectively. Growth in size, development of the process, formation of the papillae and structural differentiation of the cavernosa depend in either case on androkinin even after birth, but the os is already determined (negatively in the female, positively in the male) before birth. Thus the latter fails to develop in the masculinized clitoris but does appear in the penis of the castrate.

Determination may also account for the limitations that seem to be set to masculinization; the latter has not resulted, in any instance, in the formation of a corpus cavernosum that would completely surround the urogenital urethra. And the same applies to the behaviour of the uterus which did not show any clear influence of male hormone—a fact to which we shall have to return at a later point.

The Role of Male Hormone.

The experiments under discussion supply further evidence that the *rôle* of male hormone is the impression of male character upon the anlagen of the genital organ. In the case of the zygotic female its action upon the peripheral organs thus invokes the suppression of female differentiation or—to use this expression once more—a supersession of the female tendency of development.

The Role of Thelykinin.

As to thelykinin, the experiments support our previous conclusion—it appears, indeed, that this substance does not actively influence differentiation. The findings in oöphorectomized females show that it is not necessary for female differentiation. The experiments related above reveal the fact that female hormone cannot interfere with those slight processes of male differentiation which occur even after castration of the newborn male.

This statement may seem to be in discordance with the observations described in the preceding paragraphs, where it has been shown that female hormone actually does prevent normal male development. Yet the conclusion implying non-interference seems justified once a confusion is avoided, which was not always eliminated from previous discussions of the problem, *i.e.* the

confusion between direct action of a hormone upon the sexual characters and its action upon the gonad. In the first instance, it has been shown that the effects of thelykinin corresponded more or less to those of castration. If anything they were less severe; it is certain that the penis of the males, whether castrated or entire, injected with thelykinin, did not resemble the clitoris any more than that of a castrate. One may conclude that female hormone did not effect feminization in excess of that resulting from castration.

In the second place, it is evident that the " castration effect " is not due to direct action of the female hormone upon the genital organs of the male. When male hormone was administered to males, subjected to injections of thelykinin, a neutralization of the castration effects was obtained. This indicates that the " castration " effected by thelykinin was due to an inhibition of the secretory activity of the testes, not to interference with the effect of male hormone upon the penis; the injection of andro-kinin constituted a substitution-therapy.

Confusion would result if direct effects of a sex hormone upon the peripheral organs were confounded with indirect effects. As to the latter, thelykinin does not fail to produce them since it inhibits the activity of the testes when administered in large quantities. But it does not directly influence the " periphery ", (i.e. the extragonadic character), whereas such immediate effects are produced by male hormone. It is but reasonable to expect changes similar to those produced by thelykinin from the injection of any unspecific "antagonistic" (anti-gonadic) substance.

It has indeed been shown that the implantation of either anterior pituitary tissue or cardiac muscle in male rats aged four weeks affected the weights of the testes,[53] although it seems unlikely that cardiac muscle would contain a specific hormone affecting the genital organs. Moreover, the weight of the accessory genital organs (seminal vesicles, prostates, epididymis, deferent vessels, and penis) was significantly lower in the animals implanted with cardiac muscle than in the controls. While the observations did not refer to differentiation itself, they seem to support the present argument.

The conclusion implying the inertia of thelykinin with respect to direct action upon the periphery is further borne out by the effects of andro-thelykinin injections on intact females. The same results were obtained whether male hormone alone was administered or whether the latter was combined with very large doses of thelykinin. In either case it was only the male hormone which

produced differentiating effects; the female hormone did not manifestly interfere with the action of androkinin.

Brief reference must be made here to the general problem of sex hormone antagonism, this term being used now in its original sense. The term originally implied that male hormone suppresses the secretory activity, and indeed the development, of the female gonad and vice versa. There are not a few observations which seem to support this view; the writer's finding relating to the suppressive action of thelykinin upon the testes of the young rat belong to this group. Moore and Price[50] have adduced strong evidence for a suppression of secretory activity of the gonad of either sex by the heteronomous hormone. They have not only demonstrated and analysed inhibitory effects, but have also studied the mechanism (involving the pituitary gland) by which this inhibition is effected.

The main relevant results of Moore and Price are as follows: (*a*) "testis hormone" prevents the disappearance of castration effects; (*b*) "testis hormone" has no demonstrable influence upon oöphorectomized females; (*c*) oestrin does not hasten the involution of the male characters occurring after castration; it neither stimulates nor depresses them; (*d*) combinations of oestrin and "testis hormone" administered to castrated rats produced results attributable to the "testis hormone" component alone (six females, twelve units of oestrin each); (*e*) conversely, such mixtures when injected into oöphorectomized females, did not prevent the cornifying effect of oestrin; (*f*) oestrin, when injected in normal males (200 to 300 units distributed over twenty days) produced damage to the testis and even more marked detrimental effects in the accessory reproductive organs; (*g*) addition of male hormone to oestrin injected into entire males resulted in the persistence of normal accessory organs.

Allanson[54] failed to produce anti-gonadic effects with pure preparations of oestrin. Other authors, including the present writer, did obtain testicular inhibition. Age differences and quantitative differences may play, of course, a certain rôle in the production of anti-gonadic effects. Yet there is no need to discuss the intricate problems of anti-gonadic effects of sex hormones upon the non-gonadic constituents of the genital system; for in this respect antagonistic action of female hormone has not been discovered either by previous authors concerned with the response of the differentiated organs, or by the present writer who studied differentiation itself. Both the observations of Moore and Price[50] and the experiments related here tend to

support the view that the antagonistic effect of oestrin upon the male organs is indirect and is brought about by suppression of testicular secretion, since it can be neutralized by administration of androkinin. On the other hand, one cannot agree with Moore and Price when they conclude that androkinin has no influence upon the accessory organs of the females, masculinization of the clitoris having been demonstrated by previous authors and again in the present experiments.

To summarize, oestrin is an anti-orchidic substance, but not a direct feminizer.

As to the converse problem, the situation appears somewhat more complicated. It must be regarded as certain that male hormone is antagonistic to female differentiation inasmuch as it supersedes that inherent tendency to female differentiation which becomes manifest in the normal female, whether thelykinin be absent or present. But since female hormone is not concerned in female differentiation, it does not seem to be very appropriate to speak of antagonism between the male and female hormone respectively—this phrase being about as apt as would be "antagonism between something and nothing."

It is hardly necessary to discuss in this context the question whether male hormone possesses anti-gonadic properties (capacities of suppressing the activity and influencing the structure of, the female gonad)[53 50]. Moore and Price have demonstrated such effects which they ascribe to the suppression of pituitary secretion by the gonadic hormones. But so long as we are concerned solely with the peripheral effects of male hormone, the problem seems irrelevant. For it appears that the ovary is unnecessary for female differentiation and its suppression should not manifestly influence the course of female differentiation.

A qualification of the conclusions discussed in the preceding paragraphs may, for the moment, terminate the discussion of the problem. It has been concluded that male hormone interferes with female differentiation. In actual fact, it has been found that uterine development was normal in the animals to which androkinin was administered. Thus it might seem that the supression of female differentiation was restricted to the clitoris where it has been demonstrated without any possibility of doubt. But it should not be overlooked that the experimental females were already four days old, or even older, when they received the first injection. At this age, differentiation of the uterus is already noticeable, and determination may be advanced to a considerable degree.

VII. Theoretical Conclusions.

The Monhormonic Mechanism of Genital Differentiation.

The facts reviewed in the preceding chapters are not sufficient for the construction of a complete theory of sex differentiation, but they necessitate already a revision of some of the fundamental assumptions of the classic theories, and may serve as a basis of a new and tentative theory. If the facts are to be used for the purpose of theoretical deduction, one must be allowed to employ a certain method of reasoning. It will be submitted that the newborn rat can be likened to the rat's embryo with respect to the physiological mechanism governing differentiation of the genital system; and, pursuing this proposition even further, the newborn rat will be regarded as representative of the mammalian embryo in general.

This suggestion might seem extravagant. Differences between the newborn rat and any embryo are too obvious to demand specification. Superficially regarded, this method of reasoning may appear to be as dangerous as those comparisons between the postpuberal phase of life and intra-uterine development which form the basis of the dihormonic theories. Yet much can be said in its favour; from the purely formal point of view the method is justified if a theory of high explanatory value results. As to material arguments, it should be considered that the newborn rat, with its low state of general development, resembles the embryos of other species. One may add that the genital organs of the newborn rat are in many respects of an embryonic character; the uterus of the newborn rat resembles the Müllerian tube of the sheep's embryo (see Plate IV), rather than the uterus of the newborn sheep, which exhibits a high degree of differentiation. The same applies to other species, such as the human. Here again the differentiation of the wall of the uterus proceeds during intra-uterine development, whereas in the rat it occurs in post-natal life. As to the male, it is more difficult to make direct comparisons because of the relatively greater species differences in the structure of the genital organs. But it will be recalled that the descensus of the testes in the rat does not occur until several weeks after birth, whereas in many other species it is a feature of early foetal development; also the development of the penis in the rat is, for the greater part, a matter of extra-uterine development.

Once the fundamental hypothesis (implying the similarity of embryonic and post-foetal conditions of development) is accepted,

the conclusions reached in the previous chapters gain an obvious significance. As to the male, it would appear that genital differentiation depends on the secretion of the testis and cannot proceed in the absence of testicular hormone. Thus normal male differentiation can be regarded as the result of a reaction between the primordia of the genital system and a secretion of the male gonads. Early in embryonic development it is concluded that a hormone is secreted by the gonad of the zygotically male embryo and this hormone promotes the development of the Wolffian duct and impresses the male characterization upon the anlagen of the external genitalia.

This is all that can safely be deducted from the factual material presented previously. The fate of the primordia of the zygotic male in the primary absence of male sex hormone remains uncertain as long as only the effects of castration are considered. They would not undergo normal male differentiation; but a corresponding positive assertion cannot be made. In the experiments under discussion it was found that differentiation is inhibited by castration performed at birth; but this does not necessarily imply that castration performed during the indifferent state would lead to a persistence of the latter.

This question will arise and be dealt with later in the text—it cannot be answered by reference to the actual experiments on castration. Nor do the latter allow us to make any statements regarding the mechanism which effects the involution of the Müllerian ducts of the zygotic male. In the newborn rat the typically female primordia have already been reduced to the permanent state of rudiments, and no observation regarding the behaviour of the latter has been made. Whether the male's Müllerian ducts are destroyed by male hormone or because of the male constitution of their elements, cannot be deduced as yet.

The conclusion under discussion is in accordance with the older views. The experiments on which this discussion is based have indeed supported the contention of the dihormonic theory that male differentiation depends on the testis; they seem to show that the hormone active in early development is identical with the factors responsible for puberal maturation.

Thus it appears that the present writer's conclusions—if they can be called his—do not constitute any breach with accepted views as far as the male is concerned. On the other hand, he has to disagree with the dihormonic theories where they are concerned with female development.

It has been shown that female differentiation, as it occurs during the first weeks of infancy in the rat, does not depend on ovarian secretion—a fact revealed by two different sets of experiments, involving oöphorectomy and injection of ovarian hormone respectively. In accordance with our fundamental postulate we have to conclude from these experiments that female differentiation during the preceding phase of embryonic development is equally independent of ovarian function, and that the constitution of the genital primordia is sufficient to direct their differentiation.

It might be argued that the developmental processes occurring during the first weeks of extra-uterine life represent only the "after-effects" of a preceding phase of ovarian secretion; the latter might dominate sexual differentiation in the course of embryonic life, during which determination of the Müllerian ducts might also occur. Once determination has taken place, further ovarian secretion would no longer be required.

It is indeed impossible to refute this interpretation with absolute certainty. On the other hand, it appears to be artificial and to neglect essential rules of interpretation. It postulates, on no specific grounds, a discontinuity of behaviour of the genital organs, and conflicts with general facts of endocrinology. In the normal organism the endocrine glands do not function in such a fashion as to produce maximum effects. Addition of their products to the circulation leads to an intensification or to a change in the nature of the effect. In the newborn rat, however, one may add much ovarian hormone without influencing the initial differentiation of the uterus. Obviously, it seems unjustifiable to suppose that the ovarian secretion which has taken place before birth should be followed by a persistence of its effect at the maximum possible level. The improbability—indeed the absurdity—of such an assumption becomes even more evident when the nature of ovarian effects in general is considered; as is generally known ablation of the ovary produces, in the mature or puberal rat, almost instantaneous effects, while no effects whatsoever are detected in the newborn rat.

For reasons of simplicity, in view of the general physiological considerations, and in accordance with the principal assumption of this discussion, it may be assumed, therefore, that the differentiation in female direction of the indifferent genital anlagen occurs independently of ovarian hormones. In other words, it may be concluded that the genetic constitution of the somatic cells of the zygotic female is sufficient to invoke their female

differentiation.* The factors determining femininity become active directly in the somatic cells instead of expressing themselves via the gonad; they incite development of the Müllerian duct; they impress a female characterization upon the anlagen of the external genitalia; they may also be sufficient to effect the involution of the Wolffian system.

For theoretical purposes, the results of the experiments underlying this discussion may be exploited in yet another direction. We have seen that ovarian hormone is unnecessary for the differentiation of the female; moreover, it appears to be without effect upon the genital organs unless the latter have already reached a certain stage of female differentiation. This conclusion is necessary in view of the experiments in which oestrifying hormone was injected into newborn females and males without directly influencing development, notwithstanding the large quantities employed. In the writer's opinion considerable significance should be attached to this finding; in fact, it yields one of the key positions for the following considerations. This significance is best appreciated when the views of the dihormonic theories are contrasted with the conclusions which must be drawn from the experiments under discussion.

Those older views have been expressed in the statement that *mulier est quod est propter ovarium*. It is not only the Latin which is unsatisfactory in this sentence. Ovarian hormones do not incite female differentiation; they require the previous occurrence of female differentiation in order to be capable of exerting their typical influence. In other words, female differentiation is not an effect of ovarian activity, but a condition of the effectiveness of the latter.

It is essential that the conclusions under discussion should be fully analysed with respect to their implications. This task, however, may be postponed for the moment; at this point it is sufficient to emphasize the fact that the present writer regards female differentiation of the indifferent genital system of the zygotic female as a reaction entirely independent of ovarian hormones. It is, therefore, suggested that the indifferent genital primordia of the zygotic female would develop into an infantile female genital apparatus even in the absence of any gonad. Differentiation, in the normal zygotic female, is anhormonic, whereas in the normal zygotic male it is hormonic; these are the two main conclusions.

* To be more accurate, one should say that extragonadic (somatic) factors are all that is required to secure female differentiation.

Obviously, this theory of sexual differentiation stands midway between the opposing views of earlier students of the problem, since it accepts, in a sense, the occurrence of both independent and dependent differentiation. Needless to say, this theory represents an extrapolation of actual data (relating to infancy) into the period of embryonic development—it is not the result of a deliberate compromise between two opposed views.

So far certain conclusions have been proposed with respect to the development of the zygotic male and the zygotic female respectively. The mechanisms of genital differentiation may be regarded as essentially different. Male development appears to be the result of a reaction of a zygotic male with certain extracellular factors; female development appears to be the product of the reaction of zygotically female cells with intracellular factors or extracellular and extragonadic agents of unknown nature. Even if the conclusion to be drawn from the experiments were to be restricted to this simple statement, it would become possible to explain certain facts which were not accounted for by the older theories. But the basic facts prove to be much more interesting, and the resulting conclusions reach much further if and when the hypothesis of equipotentiality is adopted.

The conception of equipotentiality is founded on established views. It implies that the soma of embryos of either sex possesses the same developmental potencies whatever the prospective (genetically determined) sex be. The primordia of the genital system of the prospective female would develop in male direction if transported into a male environment or otherwise exposed to the action of the male, and vice versa. The theory of equipotentiality gained eminence through the work of Steinach, who stated that the exchange of gonads between male and female rats led to a "Geschlechtsumkehr," the female developing male, the male developing female characteristics. Although several authors agreed with Steinach, some of his findings have not been substantiated. Steinach and some other authors who repeated and extended his experiments overestimated the degree of transformation actually obtainable. Goldschmidt* has shown that equipotentiality is a conception which is not only justified but

*Goldschmidt does not actually speak of equipotentiality. This latter term was used by Zawadowsky. Goldschmidt speaks of the "alternative Reaktionsnorm der Geschlechtsmerkmale." (" . . . dass die erebten Geschlechtsmerkmale mit zwei Sorten von Hormonen zwei verschiedene Reaktionen eingehen können.") Goldschmidt's term, though preferable in many respects, does not lend itself readily to use in discussion.

actually necessary if genetical and physiological facts shall be brought into agreement.

But while the original conception of equipotentiality implied that the primordia of either sex would behave identically if exposed to the same sex hormone, a more formal interpretation is more appropriate. Equipotentiality should be understood as signifying identical reaction in identical circumstances. The latter may be characterized either by the presence of a specific, or by the absence of any specific hormone.

Equipotentiality of the male and the female soma thus involves identical reactions in an identical *milieu intérieur*.

Reasons for and against the hypothesis of equipotentiality have been discussed by previous authors and need not be reviewed again. It will be remembered that male potencies undoubtedly exist in the female cattle embryo (free-martin). The writer's own experiments have produced additional evidence bearing on this point by showing that the clitoris of the newborn rat can be transformed into a penis-like organ.* As to female potencies in the male, the evidence is not as convincing as in the converse case; but there are, on the other hand, no reasons why the observations of Zawadowski[57] and others should not be explained by the existence of equipotentiality.

If, therefore, the hypothesis of equipotentiality be accepted in addition to the more firmly established conclusions—detailed above, and implying dependent differentiation of the male and an hormonic differentiation of the female—certain theoretical inferences suggest themselves, or rather, become but necessary conclusions.

To begin with, it is obvious that male differentiation should occur in a zygotic female supplied with male hormone. Previous theories have adopted the same view; as has been mentioned before, the case of the free-martin strongly supports this conclusion. But the reader is particularly referred, in this context, to the experiments on masculinization of the clitoris as effected with male hormone alone. The experiment is of some interest, although it is not as impressive as the experiment carried out by Nature when she unites the chorionic vessels of a male and a female embryo; on the other hand, experimental masculinization is, in a certain sense, more reliable because the conditions of

*These experiments have corroborated the findings of previous authors who experimented on guinea-pigs. The similarity of results (cf. in Voss and Loewe[52]) adds further weight to the hypothesis that the observations on the rat have more than specific interest.

transformation have been determined, not only inferred. The significance of the observation lies, however, in the demonstration it affords of the male potencies of the clitoris. The case of the free-martin which has female external genitalia does not prove that the external genital characters differentiate independently);* the experimental transformation of the clitoris definitely shows that under appropriate conditions masculinization of the urogenital tubercle of the female is possible.

The actual conclusion thus proposed on the joint basis of the experimental facts and the hypothesis of complete equipotentiality is in agreement with a postulate of the dihormonic theories; it is submitted that the zygotic female will develop male in the place of female characters if and when it is exposed to the action of male hormone early in development. But the conditions of masculinization appear to be very much simpler than the dihormonic theories suggested. As long as a positive (feminizing) effect of the female secretion was assumed, it had to be explained why, even in the presence of female hormone, masculinization should result from the presence of male secretion (free-martin). Now it has been shown that ovarian secretion does not influence female differentiation and does not interfere with the activity of the male hormone, as can be stated in view of the masculinization of the clitoris effected by the simultaneous administration of male and female hormone, and in view of previous experiments.[58, 50] It may be repeated that there is no need to speculate on relative dominance of the male hormone or preferential reactivity to male hormones; to discuss, in an analysis of sexual differentiation, the antagonism between the male and female hormone is about as appropriate as to introduce the

*The female character of the external genitalia of the free-martin has given rise to an extraordinary confusion which has spread through the literature. Some authors argued that primordia of the internal genitalia are equipotential so that they can be transformed, in the case of a zygotic female, into male organs. The external genitalia, however, were presumed not to be endowed with equipotentiality, since even the most highly transformed free-martins still showed female external genitalia. Obviously this is a case of crass *petitio principii*. If complete transformation should happen to occur in a cattle twin (and there is no reason why it should not be possible) the resulting individual could not be recognized as a free-martin —the latter being, by definition, an individual with female external genitalia. A completely transformed free-martin would not be recognized as a free-martin any longer, it would be counted among the group of male-male twins. It could not be identified by individual but only by extensive genetical examination.

antagonism between heat and cold into a treatise on thermodynamics.

Proceeding further, the hypothesis of equipotentiality presumes that female development would occur in the zygotic male in the same circumstances which condition its normal occurrence in the zygotic female. The latter undergoes female differentiation in virtue of somatic factors, not in virtue of ovarian hormone; these factors are, however, ineffective and superseded when male hormone is present (*in sufficient concentration*). Correspondingly, one has to conclude (on the basis of the hypothesis of equipotentiality) that the cells of the extragonadic primordia of the zygotic male also carry factors which would involve female differentiation, were it not for the influence of male hormone which prevents their expression. In other words, female differentiation is assumed to result from an anhormonic state both in the zygotic male and the zygotic female; the former would undergo female differentiation were it not exposed to male hormone.

At the risk of redundancy, this conclusion must be contrasted with the views presented in the dihormonic theories. The latter submit that the female potencies of the male are manifested under the influence of female hormone; the fact that in the male partner of the free-martin no such effect has ever been observed did not deter most previous authors. The writer's explanation represents only a conclusion necessarily resulting from the adoption of the hypothesis of equipotentiality, and the findings discussed previously; in accordance with the facts the writer's explanation does not assume any active participation of female hormone in the development of femininеness; it recognizes the absolute dominance of male hormone in developmental processes and it describes the conditions under which female differentiation may occur as the *absence of any*, rather than the presence of a *specific, sex hormone*. The theory under discussion thus constitutes a physiological corollary to a genetic "presence-absence theory." Needless to say, it explains female differentiation not really by the absence of any specific factor, but assumes only the absence of any specific (gonadic) factor in the external environment of the cell. Absence of this extracellular factor (male hormone) permits intracellular factors to become effective.

It may be as well to re-state the main contents of the theory here proposed in a form chosen by Zawadowski[57] in explaining his theory of sex differentiation. Symbols such as this author used may facilitate not only the presentation of the theory, but

also the discussion of its implications which presently will have to to be undertaken.

In view of the experiments on castration one may write

$$S_m + H_m = D_m \quad \ldots\ldots(1)$$

where S_m means the soma of the zygotic male, H_m stands for male hormone; the interaction of the male soma and the male hormone effects male differentiation (D_m). Conversely, it may be stated that

$$S_m - H_m = -(D_m) \quad \ldots\ldots(2)$$

where $-$ is used to denote the interference with male differentiation effected by withdrawal of male hormone. We shall presently have to replace this "equation" by another one.

As to the female one may write

$$S_f + H_f = D_f \quad \ldots\ldots(3)$$

thus expressing the fact that female differentiation (D_f) can proceed in the presence of ovarian secretion (H_f) in a zygotic female (S_f)—a fact demonstrated (*a*) by the injection experiments described previously, and (*b*), by the findings regarding the hormone content of amniotic fluid. But one may also write

$$S_f - H_f = D_f \quad \ldots\ldots(4)$$

thus expressing the observation that the absence of female hormone (H_f) does not interfere with female differentiation. From (3) and (4) it follows that

$$S_f = D_f \quad \ldots\ldots(5)$$

which we have expressed differently before by saying that the potentialities of the soma of the zygotic female are sufficient to secure female differentiation even in the absence of female hormone.

The "equations" (1) to (5) can be simplified by the introduction of the hypothesis of equipotentiality. The latter implies that

$$S_m = S_f \quad \ldots\ldots(6)$$

This being accepted, it is no longer necessary to use separate symbols for female and male soma respectively. Substituting, according to (6), S for S_m and S_f respectively, it follows that

$$S + H_m = D_m \quad \ldots\ldots(7a)$$

and

$$S = D_f \quad \ldots\ldots(7b)$$

Instead of (*7a, b*) one might equally well write

$$S - H_m \pm H_f = D_f \text{ ; and } S + H_m \pm H_f = D_m \quad \ldots\ldots(8a, 8b)$$

which is equivalent to the conclusion that the potentialities of the soma either zygotic male or zygotic female tend to induce female

differentiation in the absence of male hormone irrespective of the presence or absence of female hormone.*

The theory developed in the preceding paragraphs differs from the dihormonic theories in that it recognizes only one hormone as an active participant in sexual differentiation. It will be referred to, therefore, by the distinctive term of *monhormonic theory of sexual differentiation*. Elaborations of the fundamental propositions of the theory will become necessary as we proceed to apply the latter; our immediate task will be completed when a schematic picture of sexual differentiation is drawn in accordance with the conclusions.

Every zygote, we submit, transmits to its daughter cells the capacity (1) of differentiating in the female direction if no male hormone, or an insufficient amount of the latter, is present in the *milieu intérieur* of the organism; and (2) of reacting with the male hormone by differentiating in the male direction. The female zygote transmits factors which impress female character upon the gonad; in the case of the male zygote factors are present which transform the gonad into a testis. These gonad-determining factors are either different from those which determine the differentiation (reactivity) of the somatic cells where they would be without effect; or else they exhibit their specific gonad-organizing activity only in the gonad, while in the somatic cells they only convey the capacity of reacting to the presence or absence of male hormone. If the gonad develops into a testis, it begins to secrete male hormone even before the testicular character is fully manifested; the male hormone invokes male differentiation. If the gonad develops into an ovary, it either fails to secrete any hormone, or else it secretes an ineffective female hormone. Absence of male hormone, in the presence or absence of female hormone conditions female differentiation.

This summary is, of course, very superficial; also, it is purely formal. But before any further elaboration of the monhormonic theory is attempted, it must be shown that the theory in its simple and primitive form can account for some of the most obvious facts of development, and for the main forms of genital monstrosity.

* Quantitative considerations have been omitted from the development of the theory. Obviously, it would be necessary to take into account degrees of hormone concentration and of cellular reactivity. But at the present juncture of knowledge and hypothesis, such quantitative considerations would necessarily be purely formal.

VIII.—Application of the Theory of Monhormonic Differentiation.

When discussing the dihormonic theory attention was directed, in the first instance, to the limitations of its experimental basis. But the main objections which were brought forward against the dihormonic theory, and which caused one to reject it, were derived from its failure to explain adequately and with reasonable economy of hypothesis, certain experimental facts, observations relating to normal embryonic development and, last but not least, teratological cases (particularly cases of lateral mosaics). It is obviously necessary to submit the monhormonic theory to the same test; while it may be maintained that it is derived from more adequate experimental data than the dihormonic theory, its ultimate justification must be demonstrated from its value in explaining independent observations made without any reference to theory.

The Differentiation of the Male.

It has been established by several independent investigators that the amniotic fluid and the embryonic portion of the placenta of various mammalian species, including cattle, sheep, horse and human, contains relatively large quantities of cornifying hormone,[59—62, 43] which is probably closely related to ovarian (follicular) secretion, since it produces the same effects. The actual quantity of hormone present varies widely with the species* and probably not less extensively with the individual; but the concentration can be very high. Thus it has been found by the present writer that 80 to 200 mouse-units of cornifying hormone are present in 100 gms. of human placenta at the end of pregnancy; other authors have estimated the yield from a full-time placenta (500 to 700 gms.) as exceeding 1,000 rat-units.[63] Its presence during very early stages of development has also been established in cattle; the concentration can be even higher, and the amniotic fluid of cows slaughtered during pregnancy is being used as the source of a commercial preparation of cornifying hormone.

The presence of cornifying hormone is not restricted to the amniotic fluid; the hormone may also enter the circulation of

* No thelykinin has been discovered in the placenta of the rat by Allen. The present writer prepared extracts from rats' placentae by extracting them with ether and acetone, but failed to obtain cornification; the largest quantity administered to one mouse corresponded to 3.4 grammes of fresh placenta.

the foetus.[64–66] It is probable that the presence of thelykinin, perhaps of placental origin, in the circulation of the foetus is responsible for the temporary antenatal enlargement of the uterus of female foetûs[67] which can be followed by post-natal bleeding resembling menstrual haemorrhage. But this effect is restricted to mature or maturing foetûs; signs of uterine activity have not been reported for foetûs less than seven months old, although during this period the thelykinin concentration of the amniotic fluid is as high, or nearly as high as, towards the end of pregnancy.

The hormone is found in amniotic fluid of foetûs apparently irrespective of sex or period of pregnancy. Thus its presence was established in six embryos ranging from 2.5 cm. to 21 cm. maximum length. None of these foetûs showed any genital abnormality; two male embryos were among those examined. It may thus be concluded that, in some species at least, normally male development proceeds, so to say, in a female medium—that it occurs while the organism is supplied with comparatively large quantities of female hormone.

The problem which arises from this fact has been recognized by several previous authors; Needham[68] formulated it in precise terms. It may be recalled that the dihormonic theories assume that female hormone is responsible for female differentiation; specific activation of vaginal and uterine elements involving proliferation and differentiation of the proliferated elements has been demonstrated in pubescent animals treated with ovarian extracts; it has also been maintained that the zygotic male can undergo a certain degree of feminization when exposed to the action of ovarian hormone. How, then, is it to be explained that in certain species every embryo does not undergo feminization although it is early and amply supplied with female hormone?

It will be seen that the occurrence of male differentiation in a female medium can hardly, if at all, be reconciled with the dihormonic theories; but it does not present any difficulty to the monhormonic theory. The latter submits that ovarian hormones are neither necessary for female differentiation nor capable of accelerating it. It was concluded that female hormone must meet with a differentiated female system in order to exert any noticeable effects, but cannot evoke the system upon which it is to act. If feminization is not an effect of female hormone but a condition for the activity of the hormone, then it is clear why a male embryo (in which female differentiation has not occurred) does not react to female hormone. In the early stages

of ontogenesis, the zygotic male like the zygotic female is indifferent, i.e. differentiated female organs are not present; in the later stages involution of the female primordia and male differentiation of the common anlagen (external genitalia) has occurred. Thus there is no stage in the development of the male embryo at which female hormone could become active with respect to the differentiation of the peripheral characters.*

This mechanism—mainly characterized by the absence of reactivity to female hormone in the indifferent or male genitalia—explains why males can develop in the body of their mother without being protected against the female hormone by a placental barrier. The equation (*7b*) may be referred to in this context.

The occurrence of feminization in male guinea-pigs and rats might be quoted in opposition to the view which is presented here, since in these experiments female characters developed under the influence of female hormone, although (according to the monhormonic theory) female differentiation should have been prevented by the action of the male hormone. But reference to the original papers (for literature see [21]) will show that most of the so-called feminine characters of the experimental animals are of more than doubtful significance, the experiments having been carried out and interpreted without due regard to the precautions necessary because of the wide range of individual variation. The only sign of feminization which has been established beyond doubt is the development of the mammary glands and mammillae of castrates carrying ovarian grafts. But it would imply complete misunderstanding of the monhormonic theory if this fact were cited against the validity of the theory. While the Müllerian duct disappears almost completely in the males of most mammalian species, this does not hold true for the mammary gland. The mammillae and mammae are organs which reach,

* The monhormonic theory explains the occurrence of male differentiation in the presence of thelykinin; but it assumes, of course, the secretion of male hormone by the foetal testes. In view of the observations described above (see p. 14) it appears surprising that the foetal testis should be capable of secreting androkinin even though fairly large quantities of thelykinin circulate through it. Species differences in the mode of reaction may play a certain rôle; but the point demands further enquiry. In this context it may be mentioned that a retrogressive phase of testicular development is said to occur in the human foetus towards the end of pregnancy; this retrogression is believed to have deceived previous authors who regarded it as permanent under-development. The alternative explanation would ascribe it to the transient, inhibiting effect of thelykinin (Reiprich).[69]

in many species, a certain degree of differentiation even in the presence of male hormone; they can therefore respond, sooner or later, to female hormone. That female hormone does not invoke the differentiation of, but only activates the already differentiated mammillae, is demonstrated by the results of experiments on rats. In the rat the male does not show normally any trace of mammillae but is said to possess mammary tissue; mammillae do not develop when male rats receive ovarian grafts or injections of thelykinin, but mammary development does take place under such conditions.[70]

In conclusion, it may be maintained that the monhormonic theory explains why males can differentiate in the female medium represented by the amniotic fluid without becoming intersexes. It explains this phenomenon without any auxiliary hypothesis, such as the assumption of specific differences between embryonic and maternal female hormones, or the existence of a *barrière placentale* (Stern) excluding female hormone.

The Effects of Gonadectomy.

According to the monhormonic theory female differentiation should occur in any embryo not exposed to the action of male hormones ($S=D_f$); so that early ablation of the gonads should result in the development of female characteristics, be the individual a zygotic male or female. On the other hand, female development cannot be expected to proceed in the absence of ovaries beyond the stage whieh is reached by the entire female before ovarian function begins to dominate uterine and vaginal development. This has been shown to be the case in the rat, which up to the age of pubescence does not react with atypical development to oöphorectomy. Yet while the gonadectomized female may be expected to develop normally up to a certain period of life, it should never develop true male characteristics. The latter, it will be remembered, are assumed to develop under the influence of male hormone, and should not appear solely because the source, potential or actual, of the female hormone has been removed.

It is unfortunately impossible to derive much information relevant in this context from the voluminous literature regarding the effects of castration and from the not less extensive data concerned with the consequences of oöphorectomy. It has already been pointed out that, in most instances, the experimenters operated on animals rather far advanced in sexual development, and that they compared the experimental animals with the controls

at a period of development when even in the female (i.e. *entire* female) the sex characters had already come under the influence of the gonad. Experiments of this description led many authors to the conclusion that either sex approaches, after gonadectomy, the type of the heteronomous sex, even though the use of the term "asexual type," which has been used for the so-called intermediate type, has been rejected on general biological grounds.[1] There is, indeed, no doubt that gonadectomized animals of either sex resemble each other to a considerable extent in the case of many species[71–74]; and it might seem that the existence of such an intermediate type opposes the view advanced in the form of the monhormonic theory.

Yet this is not the case. As has already been shown it cannot be expected that the female should continue normal development after ablation of the ovaries beyond the age at which pubescence becomes manifest. The female type is identical with the agonadic type only up to a particular (prepuberal) age which, of course, may vary considerably with the species; after this age has been reached the female hormone modifies the agonadic type to a considerable extent. Thus the pelvis assumes its ultimate proportions which are correlated to the rôle it plays in reproduction, the uterus and the associated structures are activated, and so on. Intermediation of type represented by the continued development after the age of pubescence of the agonadic type in the spayed female and the assumption of this agonadic type in the male is, of course, not in discordance with the postulates of the monhormonic theory.

To accept the latter would become impossible only if it could be shown that typically male characters (which are believed to depend on the gonad) are assumed by oöphorectomized females. But a review of the literature on the subject does not yield any instance of such behaviour. When those secondary or accessory characters are examined which are clearly sex dimorphic and thus offer a basis for comparison, it is found that the male characters approximate after castration the homologous character of the (prepuberal) female type, while the converse relation does not exist. Thus the human castrate shows pubic hair of female type, does not develop a beard, and retains the comparatively feminine voice it normally possesses during infancy; but oöphorectomy does not produce a beard or male pubic hair or a deepening of the voice. In the many species in which the female lacks the horns typical for the male, oöphorectomy does not lead to development of horns, whereas castration

interrupts or greatly disturbs their development and/or periodical renewal; so that the castrated male may resemble the female.[20, 21]

The most important material concerning the present question has been provided by the investigations of Zawadowski,[57] and among his findings those on an antelope, *Boselaphus tragocamelus*, are of outstanding significance. In this antelope the sexes differ greatly, not only as regards general appearance, but also with respect to a very noticeable sex character, namely, the colour of the coat. The hair of the male is dark grey, while the female is coloured a light red-brown. Castration of the male even at an advanced age (a year and a half) leads to the assumption by the male of the colour of the female coat and proportions corresponding to those of the female rather than the male; the development of the head-furnishings is not interfered with.

The same applies to another antelope (*Antilope cervicapra*). The male is of a dark colour, while the female is much more lightly coloured than the male. Castration carried out in this case at a comparatively early age led to the assumption by the male of the colour of the female coat.

In Ukranian cattle sex differences in coat colour are also pronounced, and again it is found that the male after castration assumes the colour of the female coat. Similar observations were made on the Banteng.

Unfortunately, the author of these most important experiments could not carry out, in some cases, the obvious control experiments represented by complete oöphorectomy of young females. However, when such experiments were carried out, it was found that the female developed body-proportions hardly different from those of the normal female, while the body-proportions of the entire male differed greatly from those of the castrated animal, the latter assuming proportions resembling the female type. Further material for such studies is provided by numerous experiments on sheep. It is generally found that the typical male sex characters do not develop after castration and that female proportions are approximated by the male after castration. But, as has been mentioned before, in most cases comparisons were made too late in life to be of decisive value.

These findings, though not sufficient to render conclusive proofs, are yet of considerable significance. This will perhaps be best appreciated if the behaviour of the mammals studied is compared with that of birds in which plumage colour is sex-dimorphic. It is well known that the hen assumes the plumage normally found in the cock when the ovary is completely

removed and restitution of ovarian tissue does not take place, while the castration of the cock does not interfere with the persistence or development of male plumage.* The latter constitutes, in most breeds, a male character which does not depend (save, possibly, for minor characteristics) on any stimulation of the feather follicles by male hormone, but represents a manifestation of potencies inherent in the somatic cells of either male or female. It seems now that in mammals the inverse condition obtains, the male assuming the female coat after castration. It may, therefore, be concluded that in those species which have been examined up till now, the female colouring which normally constitutes a manifest sex character, represents an expression of tendencies inherent in the somatic elements responsible for the formation of these characters and is not dependent on stimulation by sex hormones. This is as it should be if the monhormonic theory is correct, for the original formation of female characters according to this theory should constitute the expression of somatic faculties independent in their development of female hormones and, therefore, not be disturbed by the removal of the source of gonadic hormones. An exception to this theoretical rule might conceivably be found in species in which the anhormonic character is exhibited during infancy but modified by ovarian hormones after puberty.

Ultimately reference may be made once more to the material on which this study is primarily based. The male characteristics of young gonadectomized males should tend to disappear or to approach, where such moulding is still possible, the homologous character of the female. Theoretically one might hope to obtain a diversity of data respecting such changes since, generally speaking, the number of sex differences in mammals is very considerable. But in the very young rat the sexes are very similar in many respects in which they differ in the case of other species. In fact, certain sex differences are so slight that they are revealed only by statistical examination of a group of considerable size. This applies, e.g. to differences in the growth-rate. It has been stated that females, while born with a body-weight lower than that of the male, grow more quickly than the latter during the first weeks of life; also, the quotient body-weight divided by body-length is sex dimorphic (like the quotient body-length divided by tail-length).[12] But in view of the great variations of the actual quotients which the present writer and Miss

* This applies, of course, only to breeds where definite sex dimorphism of plumage occurs.

Sheard observed (unpublished), the experimental material is insufficient for a quantitative treatment.

Only one sex character may, therefore, be mentioned in this context. It will be recalled that the tissue constituting the corpora cavernosa shows, in many instances, though not in all regions of the glans, certain changes which cannot be reduced to an arrest of normal differentiation. In these cases a dense tissue is found which is not present in the glans of the entire male at any stage of development. However, attention may be drawn to Fig. 13 on Plate I. It will be seen that the corpus cavernosum of the clitoris shows a structure similar to that of the corpus cavernosum of the glans of the castrate. It may well be that the structure of the latter may be regarded as a manifestation of a tendency which is superseded by more intricate differentiation in the presence of male hormone, but becomes apparent in its absence so that it normally occurs in the female. On the other hand, not any change in the clitoris involving an approximation to the male or a retardation of normal development has been observed in oöphorectomized females.

Meagre as the data are, they certainly support rather than oppose the fundamental assumption of the monhormonic theory —that a tendency towards female differentiation should occur in the castrated male.

The Case of the Free-martin.

The case of the free-martin represents a weighty argument against the postulates of the dihormonic theories; it is equally inexplicable by the theories of independent differentiation ("anhormonic theories"). The main difficulty which is experienced by the advocates of the dihormonic theories when attempting to explain the phenomena occurring in the development of parabiotic cattle twins is represented by the fact that only the zygotic female is subject to transformation, whereas the male continues its differentiation without manifest disturbance.

This difficulty disappears when the facts are submitted to renewed scrutiny from the point of view of the theory of monhormonic development. In fact, unbiased interpretation of this experimental nature might have led to the construction of the monhormonic theory without reference to further facts either observational or experimental. Lillie at one time nearly reached the conclusions now derived from experimental facts by assuming that female hormone exerts its influence upon the genital system at a later time of development than male hormone. Yet

he did not follow this obviously permissible conclusion to its logical consequences and was also inclined to accept differential potentialities of the zygotic male and female respectively.

In discussing the case of the free-martin from the standpoint of the monhormonic theory of sex differentiation, it is convenient to sketch an outline of development of the genital system as it might be expected to occur when the circulations of a male and a female embryo are joined in a species in which female hormone is present in large quantities in the amniotic fluid of an embryo of either sex. According to the postulates of the theory, it must then be expected that neither embryo would react to female hormones since neither possesses differentiated female organs, while both should react to the male hormone.* It is obvious that in these circumstances male development should proceed without disturbance while female differentiation should be prevented. This is exactly what happens in the case of parabiotized cattle twins.

Thus the origin of the free-martin is regarded by the monhormonic theory as due to the influence of male hormone; in this respect the theory has nothing to add to the previous explanations. But the monhormonic theory also explains why only the female is influenced by the conditions of parabiosis with the heteronomous sex, this being due to the fundamental irreactivity to thelykinin of the undifferentiated Müllerian duct.

AGONADISM.

As has been concluded in the preceding chapter, and repeated on several occasions, the absence of the male, or indeed of any, gonad should result in female differentiation. Gonadectomy of the embryo being as yet impossible, much valuable information may be expected from cases in which not any trace of gonadic tissue can be found. Unfortunately, material of this description is exceedingly scarce; also, it has to be considered possible that gonadic tissue, while present and active during the early stages of development, may atrophy during subsequent phases of development, so that at the time of examination the individual might wrongly be regarded as truly agonadic.

Among the cases recorded in the more recent literature, the five cases of extreme sexual infantilism in the sow recently des-

* It is assumed here that during the early stages of embryonic development, testicular differentiation and function are not impaired by thelykinin, either because of low reactivity on the part of the testis or because of low concentration or absence of thelykinin (rat).

cribed by Deakin,[19] deserve some attention. In every case the external genitalia were of the *female* type; but they were very much less developed than in normal individuals. The low degree of development shown by these female external genitalia could not be referred to spaying since scar tissue was not detected.

As to the internal genitalia, the findings are not equally clear. In the place of the gonad, embryonic structures were found. The organ consisted of a dense stroma in which were embedded a number of tubules, lined by a double stratum of cuboidal epithelium. Deakin believes that these structures can be identified as remnants of the mesonephroi, not containing any germinal tissue. From his description it appears that, originating from the pseudogonads, there were present two tubes partly joined by adherence of their peripheral layers. These tubes entered the urogenital sinus separately.

Deakin considers these cases to represent truly gonadless animals. The ducts which connect the urogenital sinus with the gonad-like structures are regarded as Wolffian ducts; and some interesting conclusions are drawn by the author from his observations.

The first of his conclusions implies that the female form of the external genitalia represents the basic plan of the urinary system, and that its modelling is independent of the presence of germinal tissue. This conclusion is identical with, though worded differently from, a postulate of the monhormonic theory.* Deakin was unaware of the present writer's earlier communications in which this point of view was presented.

The second of Deakin's conclusions is perhaps of even greater interest, since it may necessitate an addition to the theory of sex differentiation. As mentioned before, the ducts found in the cases under discussion are regarded as Wolffian ducts, and it appears that no developed uteri or Müllerian ducts were found.

* Deakin is not decided as to the mechanism which links up the formation (not the differentiation) of the Müllerian ducts with the development of the gonad. In his paper (p. 367) he says: "There is a further indication that at least sufficient amounts of female hormone had not passed through the placentae to initiate the development of the Müllerian ducts . . ." This may be taken as indicating a possible influence of female hormone upon the formation of Müllerian ducts. There is not any definite basis for this assumption, for Müllerian ducts are laid down, e.g. in the rat, in embryos of either sex although female hormone is not demonstrable in the placenta, amniotic fluid, or embryo. However, the question is not of immediate concern at present, when we are dealing with the *differentiation*, not the *formation*, of the Müllerian duct.

Deakin is inclined to regard the formation of the anlage of the Müllerian duct as dependent on the presence of, or as homodynamous with, the formation of true gonads (which, needless to say, may be of either sex. (See also [75]).

It is obvious that the cases described by Deakin support, to some extent, the monhormonic theory which assumed female modelling of the anlagen to occur in the absence of gonads. Attention must be drawn, though, to a deviation of the observed facts from the expectations. According to the monhormonic theory, the Wolffian ducts should disappear completely in the absence of male secretion, whereas, in the cases under discussion, embryonic organs were found which could be regarded as remnants of the Wolffian ducts. However, cases of similar nature will have to be discussed below, and a tentative explanation will be offered.

Very numerous cases of agonadism have been reported in human subjects, and several extensive reviews on this monstrosity have been published.*[75, 76] Critical students of the subject agree that the complete absence of the gonads has not been established with anything approaching certainty in the vast majority of cases; much less has it been, or could be, shown that the individuals in question were agonadic *ab initio*. A few cases which a recent reviewer[77] regarded as probably agonadic were all women of the infantile type. To refer to only one instance[78] it was found that a subject exhibiting general dwarfism lacked any trace of ovarian tissue detectable even by detailed histological examination; the genital organs were completely female, but their development did not exceed the infantile level. The female character of this case, as of many others, would seem to support the theory under discussion; it is interesting to note that, in the present writer's knowledge, a convincing case combining regular male development of the genital organs with anorchy has not been described, and that the great majority of so-called agonadic cases were of completely female type. On the other hand, the number of female subjects examined with respect to their genital development probably vastly exceeds, or exceeded during the past centuries, that of male subjects similarly observed; so that the numerical relation is of doubtful significance. In addition, cases of agonadism should never with confidence be regarded as primarily agonadic, as has been mentioned

* It proved impossible to refer to the original publications of all cases mentioned in these reviews. Kermauner's review was mainly relied upon since its author possessed a very full knowledge of the subject and teratology in general.

before. Thus these cases are of value for the problem under discussion only in so far as they fail to produce difficulties for the monhormonic theory, a definite instance of complete agonady and concomitant male differentiation not having been established. (Baer[87].)

Hypospadias Peniscrotalis and Pseudo-hermaphroditismus Masculinus Externus.

The literature on *hermaphroditismus* in human subjects contains numerous descriptions of cases in which a normal apparatus of male internal genitalia was combined with external genitalia of more or less definitely female character.[79, 21, 80] The various types can easily be arranged in a natural series ranging from the development of a completely female external genitale to slight abnormalities such as hypospadias penis.[1] Thus in a certain case,* the external genitalia were indistinguishable from those of a normal woman. In similar cases a large central sinus urogenitalis was present; the phallus was represented by an organ differing but little from a clitoris, its resemblance to a penis being restricted mainly to the appearance of a navicular fossa and a shallow sulcus originating in the latter. The labia minora were identifiable as the marginal regions of the urogenital sinus and labia majora were present instead of a fused scrotum. Yet testes were found within these labia majora, which thus combine the function of a scrotum with the appearance of its female homologue.

Femininity is displayed to a lesser degree by cases which, though differing in details, may be grouped under the term *hypospadias peniscrotalis*. It is generally known that this term is applied to malformations characterized by a transposition of the orifice of the urogenital sinus from the fossa navicularis to the distal portion of the ventral surface of the corpus penis. This malformation is combined with incomplete, or lack of, fusion of the two scrotal anlagen. Hypotrophy of the penis and the development of a slit-shaped opening of the sinus urogenitalis enhance the female character of the resulting external genitalia. It has rightly been remarked that this monstrosity "has its prototype in the development of the female genital organs" under normal conditions.

Ultimately the similarity between such abnormal male and the normal female organs may be restricted to a simple transposition

* See "Beobachtung 1244" and index in Neugebauer's book.[80]

of the opening of the urogenital sinus to the corpus penis. More about this type (hypospadias penis) will be said below.

When attempting to explain these monstrosities on the basis of the monhormonic theory, it will be accepted, in accordance with Goldschmidt, that the external genitalia not only undergo differentiation rather early in development, but also reach their determination point comparatively soon. Both embryological findings and the study of the free-martin support this conclusion even though it may not be acceptable without certain qualifications necessitated by the transformation of the clitoris long after normal differentiation has completed its course.*

Having accepted the principle of early determination, the interpretation of the type under discussion may be based on considerations dealt with previously, and concerned primarily with the development of the genital organs in the absence of male hormone. The conclusion was that in these circumstances, female development of the genital anlagen would result.

Be it now assumed that for some reasons (such as disease or inherited abnormalities retarding the rate of gonadic differentiation) the gonad of a zygotic male does not secrete male hormone at the stage at which this secretion normally occurs. The anlagen of the genitalia which attain determination during this phase of "absence of male hormone" will undergo female differentiation. When utimately testicular secretion does begin, the external genitalia may already have developed sufficiently to be determined; while the internal genitalia are still "pliable" the external genitalia can no longer react fully to male hormone. Thus the internal organs may assume male, the external female character.

It seems that certain facts are indeed in favour of an explanation of this type. Thus it is well known that a general retardation in the development of the testicle has been observed in some of the cases under discussion. In some instances this retardation led to what is known, in the medico-legal literature, as *erreur de sexe*. It has happened that individuals were regarded as females because of the female character of their external genitalia. Yet at the age of puberty, not infrequently when some accident intervened, organs suddenly appeared in the labia majora which were ascertained, by surgical or other method, to be testicles.[80] This delayed descent of the testes can be preceded or followed by development of secondary male characters (hair, etc.) which then

* This is one of the reasons why an alternative mode of explanation has been offered below (cf. p. 57).

confirm the diagnosis of *erreur de sexe*. The delay in the descent may be regarded tentatively, as supporting the assumption that the factors responsible for the elaboration of male hormone did not come into operation at the normal stage of development; in this context, it may be mentioned that the factors which invoke testicular secretion are also responsible for the descent of the testes or at least closely associated with the latter. For it has been shown that gonadotropic extracts which stimulate testicular secretion also hasten the descent.[82]

The explanation offered here for the origin of peniscrotal hypospadias and related monstrosities differs in some important respects from the interpretation set forth by Goldschmidt, even though it is indebted to him for the concept of the time-factor. Goldschmidt regards abnormalities of the type under discussion as grades of intersexuality. We regarded the abnormal individuals as genetic males; Goldschmidt believes that they are genetic (zygotic) females. They begin development, he thinks, as females so that the gonad initially secretes a female hormone. The female character of gonadic activity persists for a certain period, and the external organs which attain determination (if not differentiation), during this initial period are assumed to display female character. The end of the initial period is marked by the "Drehpunkt" when the gonad assumes male character, and secretes male hormone, thus enforcing male differentiation of all internal primordia not yet fully determined at the time of the "Drehpunkt."

Needless to say, Goldschmidt's theory may be shown to be justified by future investigations. But, the possibility of the peniscrotal hypospade being a zygotic female can well be reconciled with the monhormonic theory; it is only necessary for this purpose to omit from Goldschmidt's theory the assumption—which, we believe, is unwarranted—that a female hormone secreted during the first (female) phase of gonadic activity influences genital development, and to realize, instead, that the individual, before reaching the switchover point in its development, is uninfluenced by female hormones and differentiates entirely under the direction of intracellular, or non-gonadogenous extracellular factors.

However, certain serious difficulties against Goldschmidt's interpretations are encountered in any attempt to fit cases of hypospadias penis into the Goldschmidt-scheme of female intersexuality.

The reader is reminded that hypospadias penis is a term

applied to a genital abnormality in which, as in hypospadias peniscrotalis or perinealis, the opening of the urogenital sinus is not situated at the fossa navicularis, but is transposed towards the root of the phallus; on the other hand, fusion of the genital folds has occurred so that a scrotum is present. Now it seems reasonable to regard hypospadias penis from the same point of view as hypospadias peniscrotalis, since the differences are only differences of degree, not of kind.

The monhormonic theory explains indeed hypospadias penis in the same way as the more pronounced peniscrotal type of abnormality. A hypospadiac penis is expected to develop if and when testicular secretion is delayed by a very short period. The phase of female differentiation would then be long enough to influence to some extent the character of the orifice of the sinus urogenitalis; but too short to prevent fusion of the genital folds under the influence of male secretion.

Thus hypospadias penis can be referred to the same factors as hypospadias peniscrotalis if the monhormonic theory is applied; Goldschmidt's theory, on the other hand, fails to account for the two types by a common explanation. If the individual afflicted with hypospadias penis represents a zygotic female, then he could beget only daughters.* This is obvious; the constitution of the female mammal being (XX) as far as we know, the hypospadiac would produce only spermatozoa containing one X-chromosome (neglecting the possibility of non-disjunction). Therefore, *all* ova fertilized by the hypospade's sperm would attain the constitution (XX) and would develop into females.

In actual fact, it is well established that individuals exhibiting hypospadias penis can beget normal sons[83, 1]; there is, therefore, no reason to assume that Goldschmidt's explanation of hypospadias peniscrotalis is applicable to the milder form which does not lead to infertility.[34]

Nor is Goldschmidt unaware of this difficulty; in fact, it must be clearly understood that he was the first to recognize it (Goldschmidt, 1927, p. 313). He mentions that the recorded pedigrees of hypospadias penis do not agree with the assumption that the hypospadiacs are zygotic females; it is also improbable that intersexuality should be so frequent as to account for the numerous instances of hypospadias (one in 300, Goldschmidt, *loc. cit.*).† Goldschmidt, having failed to account for hypospadias on the basis of his general theory, considers the possibility

* Or hypospadiacs representing intersexual (zygotic) females.

† Which is frequently inheritable.

of hypospadias penis representing a hereditary abnormality, not necessarily involving other sexual abnormalities; it may be due to the action of genes of purely local effect, and belong to the same class as, say harelip.*

Needless to say, this alternative can by no means be excluded; nor can any decision of this question be expected until experimental investigations have been carried out. At the present moment, it may be claimed, though, that the monhormonic theory can account for hypospadias penis without any artificiality, but simply by assuming that the inception of testicular secretion may be delayed for a very short period—a period which is yet long enough to permit the initial differentiation of the sinus urogenitalis and the urogenital tubercle to proceed in female direction.

This, then, is the result of the analysis. There exists a natural series of abnormalities of external genitalia in individuals with male internal genitalia ranging from hypospadias penis (the mildest form) to complete femininity of the external organs. The explanation offered by the monhormonic theory for the various types corresponds to their position within this series; the mildest forms are due to slight, the most pronounced forms to prolonged, delay in the inception of testicular secretion. Thus the variations are explained by differences in a quantitative factor—the extent of the period of delay—and it appears unnecessary to invoke different explanations for the mildest form of abnormality. A specific general statement is not made as to the genetic nature of the abnormal individuals; they may be genetic males with delayed inception of testicular secretion or genetic females† who have undergone a switchover during development. The phaeno-typical effect should be the same as far as the female system is concerned.

Ultimately attention may be drawn to the similarity between the type of abnormalities which have been considered in the preceding paragraphs on the one hand, and the free-martin on the other hand. In either case a combination of external characters of more or less feminine character with internal genitalia of male type has been encountered. While the explanation of the two cases differs inasmuch as in one case, an intra-organic source of the male hormone has to be assumed, while in the other case male hormones are supplied from without the

* Moszkowicz is less discerning than Goldschmidt. He lists hypospadias penis as a mild form of female intersexuality.

† In the case of hypospadias peniscrotalis.

abnormal organism, it will yet be realized that both types support the view that the external genitalia not only differentiate before, but become at least partially determined before, the internal genitalia, a conclusion which is in accordance with embryological data. If Goldschmidt's interpretation, which implies that the cases of hypospadias are zygotically female, should prove correct, then it would have to be concluded that genetic females can develop completely male external genitalia (as in hypospadias) which approach the male type more nearly than is the case in most free-martins. If our simpler explanation invoking only a delay in the inception of testicular secretion should be corroborated by future researches, then it would appear that in a male organism completely female external genitalia can develop. In either case the theory of equipotentiality and the theory which ascribes the female character of the external genitalia of the free-martin not to a specific difference in the respective developmental mechanisms of the external and internal genitalia, but to the operation of a time-factor, gains in probability.

Intersexes in Animals.

Abnormalities resembling, or actually identical with, hypospadias are not restricted to the human species; apart from the free-martin with its different ontogenesis, numerous instances of similar aberrations from the normal have been described in horses, goats and pigs.[85, 86, 87] The most interesting material has been supplied by Baker[88–90] in his descriptions of a series of "intersexes" in the pig.

In these animals the internal organs were always essentially male though some of the male organs were often poorly developed or absent. Uterus and vagina were not found, but the external genitalia varied from nearly the female condition to something approaching the male. A complete and apparently continuous series can be established leading from a male with almost completely female external genitalia to an intersex which is but slightly different from the normal male.

The explanation offered for these cases on the basis of the monhormonic theory would correspond to the interpretation of the cases of hypospadias peniscrotalis. It may be assumed that testicular secretion did not begin until comparatively late in development so that the external genitalia could differentiate in female fashion. Baker himself has offered exactly the same

explanation* so that there is no difference between his and the writer's point of view, except that the latter has generalized this conclusion for all female organs in view of his experimental results.

The findings on the testicles of the intersexual pigs of Baker's series support the view that the female differentiation of the external genitalia is due to delayed inception or lack of testicular secretion. In those cases in which the female character was most pronounced, the testicles proved to be abnormal, not showing any spermatogenesis but few abnormal interstitial cells (Leydigs' cells). However, when the female character of the external genitalia was but slight, the testicles proved to be normal.

Hermaphroditismus Masculinus.

Peniscrotal hypospadias and similar types of abnormality have been explained on the basis of the theory here propounded as caused by a delay in the inception of testicular secretion. In order to account for the facts it was assumed that this delay is terminated sufficiently early to bring the development of the internal genitalia under the influence of male hormone. But the latter condition may conceivably not be fulfilled; the delay may be prolonged so that the differentiation and corresponding activation of the testicle do not occur until late in development; we would then expect, according to the theory, that during this early anhormonic phase even the internal genitalia would differentiate more or less completely in the female direction. If male hormone begins to be secreted before the Wolffian ducts have undergone involution to which they are doomed in the absence of male hormone, residues of the Wolffian ducts, or even a completely developed vas deferens and epididymis should develop, associated, of course, with uterus, vagina and female external genitalia. On the other hand, if testicular secretion does not occur until after the involution of the Wolffian ducts is completed, it would result in the development of an individual with male gonads and female genitalia.

Thus a moderately prolonged delay in the inception of the production of male hormone should result in individuals who have, without exception, testes and female external genitalia,

* Baker[30] adds in a footnote that conceivably the female differentiates under the influence of the ovarian hormone. Thus he does not seem to be decided in his views; he was unaware of the present writer's work[4, 5] when reporting his findings.

but vary as to their internal constitution; the latter may be characterized by (*a*) well-developed and functional male organs with rudimentary uteri (*uterus masculinus*); or (*b*) the presence of both sets of organs either being functional or non-functional, or (*c*) the presence of female internal genitalia with or without rudiments of the Wolffian ducts. It will readily be seen that these types which are, of course, not sharply divided, correspond to the types classified in the medical literature under the heading *Hermaphroditismus masculinus*.

Once more reference may be made to Goldschmidt's theory of intersexuality, as applied to the cases under discussion. The explanation given by this author is, of course, essentially the same as that offered for peniscrotal and perineal hypospadias, the only difference being that the switchover point is supposed to have occurred later in development. Individuals, abnormal in that they possess male gonads but female external genitalia associated with female internal organs and residues of, or functional derivatives of, the Wolffian duct, are thus regarded as genetic females. Their gonad is supposed to have been initially of female character, but to have undergone sex reversal early in development. At the risk of redundancy, it may again be emphasized that Goldschmidt's interpretation of these cases may prove to be correct. This would not imply an error in the theory of sex differentiation as advocated in these pages. The monhormonic theory would still simplify Goldschmidt's theorems inasmuch as it ascribes the female development, occurring during the first phase of differentiation, not to an embryonic hormone of the gonad, but to somatic, intracellular factors. Generally speaking, the explanation submitted by the present writer is indebted to Goldschmidt for one of its basic principles, namely that of the time-factor; on the other hand, it does not depend, as is the case with Goldschmidt's theory, on the confirmation of the somewhat doubtful assumption that all genital monstrosities of the type under discussion represent intersexes—in particular, individuals who are genetically female, but undergo sex reversal. The following summary may help to clarify this point; it is based on Moszkowicz's table of intersexuality. The author shows what has to be expected according to Goldschmidt's theory if sex reversal occurs in a genetic female at various stages of development. For the present purpose only one case need be considered (alteration of the direction of development early in the third month of intra-uterine life of human embryos).

(*a*) Goldschmidt's original scheme. (Genetic female). First

two months of uterine life: female character of the gonad: secretion of female hormone: therefore female differentiation of the genital anlage. End of second month: Switchover, and subsequent secretion of male hormone. The latter advances the development of the Woffian ducts but cannot greatly influence the external genitalia nor destroy the Müllerian tubes completely because of partial or complete determination having occurred in these organs. Result: Hypospadias perinealis; uterus and tubes present; Gaertner's tubes in place of *vas deferentia*; gonad of testicular character but hypoplastic and abdominal.

(*b*) Goldschmidt's scheme combined with the postulates of the theory of monhormonic sex differentiation (zygotic female). First two months of intra-uterine life; female development of the gonad. Not any secretion of, or effect of, female hormone. Female development of the anlagen due to somatic factors. End of second month: Switchover in gonad; secretion of male hormone; subsequent development of internal organs in male direction, but persistence of female character of determined organs (external genitalia). Result: As under (*a*).

(*c*) Possible scheme: Genetic nature of individual: male. First two months: delayed differentiation and/ or activation of the testis; therefore, no secretion of male hormone. Consequently female direction of differentiation as under (*a*) and (*b*). End of second month: Differentiation and activation of the gonad; therefore secretion of male hormone and consequently male differentiation during the subsequent phases of development. Result: As under (*a*) and (*b*).

The structure of the gonad (ovotestis) in certain, but by no means all, of the abnormal cases under discussion favour Goldschmidt's interpretation which implies female intersexuality. On the other hand, if it should be definitely proved that we are justified in ascribing female differentiation to somatic factors acting independently of the gonad, scheme (*c*) appears to be not improbable, for there is nothing inacceptable in the assumption that testicular activity may be delayed developmentally. Since the nature of the factors responsible for such a delay is, of course, unknown, one might transgress the field of facts and have recourse to speculation. Thus it might be suggested that the embryonic secretion of the testicular hormone depends on the secretion of the anterior lobe of the pituitary as is the case in extra-uterine life.[82, 91, 32, 93, 94, 85] The pituitary is apparently subject to hereditary abnormalities of function; it has been plausibly suggested by Crew that the development of the various

breeds of domesticated animals was largely attained by selecting mutants affecting the pituitary. Some such mutant may be characterized by a delay in the inception of the secretion of the gonadotropic hormones, thus causing abnormally late secretion of testicular hormones and, indirectly, the development of genital monstrosities. A mutant form of this type could, of course, not beget any offspring save in the mildest forms (hypospadias penis); yet the suggestion may be open to experimental investigation since it might be possible to prevent the development of the pituitary in mammalian embryos; if our theory is correct this operation should result in male intersexuality (i.e. in the development of individuals with female differentiation but sexual infantilism caused by pituitary deficiency).

Cases of the type analysed in the preceding paragraphs show many peculiarities with respect to the structure of the genital system, and it is not possible at present to offer other than purely speculative explanations for the many minor deviations from the theoretical expectations. Nor does the subject call for such an explanation, since none of the particular features of the cases under discussion places any definite obstacles in the way of the theory, so far as the present writer is aware. Only one fact demands attention, and must be discussed briefly.

Uterus Masculinus.

According to the theory under discussion, the Müllerian tubes should persist, and develop into uteri, or a uterus, if and when testicular secretion does not begin at the normal time and is delayed beyond the stage at which the ducts attain determination. On the basis of the experimental findings one would not expect these persistent Müllerian ducts in a male individual to become fully mature at any time of life; for maturation of the uterus, unlike its differentiation, depends on ovarian hormones. But in actual fact, monsters have been described which, generally speaking, fall into the category discussed above, but differ from the majority in that they possess a well-developed and apparently fully functional uterus. It is true that the function of these male uteri has never been examined in detail and with due reference to the more recent knowledge of uterine physiology; but the illustrations given by some authors leave no doubt that the uteri of some abnormal males were exceedingly well developed. This applies particularly to intersexual pigs. The reader is referred to the illustrations in the reviews published by Meisenheimer and Goldschmdit[21, 1], and reminded that the

uterus, of the pig oöphorectomized during infancy, becomes "coiled into small knots and embedded with fat and peritoneum."[34] The uterus of the intersexes in question certainly does not fit this description.

However, it has been shown by recent researches already referred to previously in this essay, that the normal male may produce certain quantities of ovarian hormone. Oestrifying substances, probably identical with those detected in the urine of the female, have been extracted from the urine of normal men and testicles of domesticated animals.[96, 97] Let it be assumed that the differentiation of the uterus, in cases in question, was not interfered with because of delayed inception of testicular secretion. The uterus would then be permitted to reach the phase of reactivity—i.e. the stage in which it can react with maturation to the presence of female hormone. If the testes of the intersexual individual, like those of normal animals, would produce female hormone, the differentiated uterus might undergo that impressive development which it actually displays in some cases described in the literature.

This explanation is offered purely as a suggestion but, however much diffidence may be felt as to its actual justification, it should demonstrate that the cases under discussion can be reconciled, in principle, with the postulates and conclusions set forth previously.

Alternative Interpretations.

The types of genital monstrosity discussed in the preceding section of this chapter were explained by the operation, in a monhormonic mechanism, of a time-factor in Goldschmidt's sense; this explanation retains its validity, for the present, whatever be the genetic sex of the individual in any particular case. Numerous abnormalities can thus be accounted for. But there exists a group of monstrosities of different structure which do not fit the explanation previously propounded.

The simplest type of this group is represented by individuals in which a complete and functional male apparatus (external and internal) is combined with a *uterus masculinus*. We do not refer, of course, to males of those species in which a uterine rudiment is present normally in every male,[21] but only to the far more numerous forms in which, normally, a uterus is developed only in the female. Monstrosities of this type have been described in various species including the human. The reader is referred for examples to Neugebauer's book. Such mosaics are

of interest because they cannot be regarded as the product of a delayed inception of testicular secretion conditioned by delay in testicular development in a zygotic female; nor can they be explained by the assumption of male intersexuality. This is readily shown by a detailed analysis:

(*a*) If testicular secretion occurs with a certain delay in a zygotic male, then the external genitalia which appear to become determined very early in development, should be affected in the first instance and should become female. We are dealing, however, with individuals which have normal *male* external genitalia; it is only the Müllerian ducts which are abnormal; they have failed to undergo that atrophy to which they are normally subjected in the presence of male hormone. It is impossible to assume that the secretion of male hormone occurred early enough to direct the male differentiation of the external genitalia but ceased subsequently, for the Wolffian ducts (which differentiate after the external genitalia) are functional in the individuals in question.

(*b*) It is equally impossible to regard the individuals in question as female intersexes; if they are zygotic females in which an early switchover has occurred, it must be assumed that the switchover occurred early enough to impress male character upon the external genitalia; yet the female organs did develop *after* this initial phase of male differentiation.

(*c*) The individuals might be zygotic males in which a switchover towards femininity has occurred. Then it would follow that the switchover had occurred too late to prevent the external genitalia from assuming male character; it must have occurred early enough to effect development of the Müllerian ducts or, at the very least, to prevent their involution. If this were true, then it could not be explained why the female phase following upon the "Drehpunkt" did not prevent the development of the Wolffian duct.

This analysis of the explanations, apparently possible on the basis of the theory of intersexuality, reveals the inadequacy of the latter; it is significant that the type of monstrosity under discussion does not find any place in the otherwise complete table of intersexuality given by Moszkowicz. A different explanation is thus called for, and we shall now show that the theory propounded in these pages can supply it.

In evolving our interpretation, we shall make use of a proposition of the theory which was derived and formulated previously, but has not yet been reduced to its implications. On

the basis of the experimental findings, it was concluded that male differentiation represents the product of a reaction between cell and male hormone; the symbol

$$S + H_m = D_m$$

has been used. The timely secretion of male hormone is thus to be conditional of normal male development; but so is, obviously, the proper reactivity of the somatic cells represented in the symbol by (S).

Now it is well known that reactivity to any hormone varies very widely. No instance of an all-or-none effect of a hormone has ever been established; some authors claimed to have demonstrated the action of this law in the case of hormonic effects[95]; but they employed inexact methods, and their views have but historical interest.[44] Hormonic effects can be graded by varying the dosage of hormone in question.[99, 100, 101] On the other hand, the effects of a given amount of any hormone vary with the individual. The degree of variation depends presumably on the genetical character of the recipient, on the absolute quantity administered and on numerous other factors, many of which are not controllable in actual experimentation. All this is common knowledge and almost platitudinous; detailed discussion is certainly not required. As to the particular case of male hormone, the reader is reminded that the procedure followed in its standardization constitutes itself a demonstration of differential reactivity. What is called the "unit" of testicular hormone is a purely statistical measure; it is the quantity of hormone which, under standard conditions of administration, will produce a quantitatively defined average effect in a group of animals. It has been proposed, e.g., to regard that quantity as a "unit" which will cause, within a certain period, an average increase (of 50 to 20 per cent) in the comb area of three white Leghorn capons.[102] The problems with which attempts at standardization are confronted are mostly created by variability; while one animal may react with pronounced effects to a fraction of the unit dose, another may require a multiple of the latter to show the same effect.

In our own experiments variations of the reactivity to male hormone have become obvious in the case of the response of the clitoris. It has been related that two out of seven females in which male hormone was administered did not respond with the development of the anterior process, which occurred in the remaining five animals. It cannot be assumed with certainty that larger doses would have produced this effect in the two

refractory animals which showed other signs of masculinization; but in view of general experience with preparations of hormones this is likely.

The variation in reactivity to male hormone is of no great interest if considered only as a phenomenon *per se*. If, however, the data relating to the transformation of the clitoris into a peniculus are considered in a different light, variations in reactivity to male hormone (referred to, subsequently, as H_m reactivity) gain considerable importance.

The probability that the transformation observed in the experiments was a product of other than experimental conditions, is extremely small; conversely, the probability that normal female differentiation would have occurred under normal conditions, is extremely high. In other words, it is very highly probable—so probable indeed as to amount to certainty—that all seven animals which survived the administration of male hormone possessed the potency of developing a normal clitoris.

The implications of this conclusion which may be regarded as well-established in spite of the small number of cases observed, will be more clearly realized if a different formulation is chosen. We may say that H_m-reactivity can vary widely in a group of animals all of which are fully capable of developing normal female characters in the absence of male hormone. Normal genetical constitution of the cells, without any specific extracellular stimulus, is sufficient to invoke female differentiation; but this normal genetical constitution of the cell, which conditions its inherent tendency to female differentiation, does not imply a uniform degree of H_m-reactivity.

It is now necessary to trespass from the region of well-established fact into the field of hypothesis. We have seen that in some cases H_m-reactivity is lower than in others—that, in some individuals, larger quantities of male hormone are required than in others in order to supersede the female tendencies. It is no more than probable that genetical or environmental circumstances may lower the H_m-reactivity well below the normal level. In other words, the threshold of concentration of the male hormone may conceivably rise so high that the quantity of hormone provided by the testes is insufficient to procure male differentiation. But since female differentiation may occur even when H_m-reactivity is low, it would follow that a primordium with abnormally low H_m-reactivity may differentiate in female direction even though male hormone circulates in such

concentration as to impress male character upon primordia with normal H_m-reactivity.

Returning now to the problem of the origin of the *uterus masculinus*, it has to be remembered in the first instance, that male differentiation does not always imply a process of development *sensu stricto;* in the case of the Müllerian ducts H_m-reactivity conditions the involution of the primordium. Absence of H_m-reactivity would conversely effect the persistence and differentiation of the Müllerian duct in the presence of male hormone, just as low H_m-reactivity permits the continued development of a clitoris even in the presence of an amount of male hormone sufficient to procure the formation of a peniculus in most individuals. Be it submitted, therefore, that in the monstrosities in question (types of *uterus masculinus*) the constitution of the primordium of the Müllerian duct was abnormal. The capacity for female differentiation may have been unimpaired; but in consequence of some somatic loss—mutation or some hereditary abnormality or even purely environmental circumstances—H_m-reactivity was absent or weakened. This abnormality being restricted to the Müllerian ducts, normal male differentiation of the other genital primordia would result, while Müller's duct would not react to the male hormone and thus fail to undergo involution.

It is submitted that this hypothesis represents no more than a legitimate interpretation of observed facts; on the other hand, it will be necessary to determine in future experiments the degree of variation of H_m-reactivity; it seems of interest to establish the lowest degree of, and the genetic behaviour of, H_m-reactivity in any random group of normal females.* Such detailed information might facilitate an estimate of the probability of the occurrence of extremely low H_m-reactivity; but it is not necessary for the acceptance of the main conclusion.

Although our conclusion is hypothetical and nothing of a factual nature can be added to its experimental basis, a more detailed analysis is advisable since it may point the way for experimentation.

(*a*) It will be recognized that the assumption of the purely intracellular nature of H_m-reactivity constitutes, in all probability, a simplification of actual conditions. Reference to other hormonic effects shows that reactivity is frequently determined by rather complex conditions. Thus both granulosa and theca of the ovarian follicle undergo luteinization, in the

* Such experiments were planned but proved prohibitively expensive.

pubescent rat, if a certain quantity of gonadotropic hormones prepared from the urine of pregnant women is injected. If the same preparation is administered to very young females, only thecal luteinization is effected. This lack of reactivity on the part of the granulosa has been ascribed to the absence of a synergist of pituitary origin. If this should prove to be the case, reactivity would be conditioned, at a certain age, by an extracellular factor. In still younger (newborn) rats even the combination of anterior lobe extracts and urine preparations fails to invoke luteinization; this may be due to the absence of yet another extracellular sensitizer or to the lack of intracellular reactivators. Similarly, it is by no means certain that the factors determining the H_m-reactivity in the clitoris (or, for that matter, in any genital primordium) are situated exclusively in the cells of the primordium itself. For our problem, the distinction between intracellular and extracellular conditioners is of secondary interest; but an investigation concerned with this alternative might bring to light mechanisms of importance in sexual differentiation.

(*b*) We have based our interpretation on the theorem of the "alternative reactionsnorm." We have assumed, without expressly re-stating this fundamental postulate, that there exists a gene or a group of genes, which confer upon the cell the tendency for female differentiation. These genes would effect female differentiation if and when male hormone is absent or present in but small quantities; they would enforce male differentiation of the cell when the male hormone exceeds a certain threshold. This theory can easily be reconciled in two ways with the major conclusion, implying variations in the degree of H_m-reactivity; (i) invoking Goldschmidt's quantitative theory of the gene, it might be assumed that the gene-group responsible for the female tendency of the somatic cells can vary in valency and would accordingly demand a greater or lesser concentration of male hormone before male differentiation can result. (ii) Similarly, the theory of the genic balance can be used as a basis of explanation; H_m-reactivity may be due to a certain genetic situation which can be disturbed in such a fashion as to permit female differentiation while H_m-reactivity is lost.

It may be mentioned, however, that recently a modification to the original theorem of the "alternative reactionsnorm" has been offered by Danforth[109a] This author shows that alternative sexual differentiation can be ascribed in principle to the action of different genes or groups of genes. In Danforth's

scheme one gene (responsible for female differentiation) becomes active under one set of conditions, the other gene, which determines masculinity, under a different set. These conditions are represented, of course, either by sex determiners active within the cell, or by extracellular hormones, or by the absence of any specific condition. If future researches should indicate that the characters represented (*a*) by the phenomena of female differentiation and (*b*) by H_m-reactivity respectively, may segregate, Danforth's theory would appear to be substantiated. For the problem under discussion the ultimate decision between the original and the modified theory may be awaited with interest; if Danforth should prove to be justified, the loss of H_m-reactivity might be ascribed to the elimination of those genes which, in the presence of male hormone, effect male differentiation.

The hypothesis implying complete loss of H_m-reactivity constitutes only an extrapolation of the actual data pertaining to the variation in this character. Yet it may seem a strange theorem to the reader who is not acquainted with this field of research; it may be appropriate, therefore, to break, for once, the self-imposed methodical rules of this essay and to refer briefly to certain mechanisms governing the development of sex dimorphic plumage since there a parallel will be found. It is generally known that in most breeds of fowls, the male differs widely from the female plumage. The male type is identical, apart from comparatively unimportant features, with the anhormonic form—it develops in the male, not because testicular hormone is present, but because ovarian hormone is absent; it appears in the female after complete oöphorectomy. But regional differences are pronounced when different breeds are compared. Thus the saddle feathers of the *Mille fleur* are sex dimorphic, being "long and copious" in the male, while the sickle feathers are only medium in length and slightly curved. In the Campine, the saddle feathers of the male are "scarcely distinguishable from those of the female, whereas the sickles are of good width, well curved, and extending beyond the main tail feathers."

In either breed, any feather approximates to the male form in the absence of ovarian hormone; on the other hand, regional feathers may respond to ovarian hormone in one breed but not in the other. The constitution of the feather's follicle in the saddle of the Campine and the tail of the *Mille fleur* conditions the absence of specific reactivity to female hormone even though

the capacity of specific anhormonic differentiation (=male type) is retained.

Different amounts of oestrin are required in order to feminize the feathers of different regions. "Gradual increase in the amount of ovarian hormone administered converts progressively the feathers of one part after another from the male to the female type" (Danforth), always supposing that the follicle is capable of reaction.

The American workers have not only supported and refined the earlier theories of the rôle of the threshold in the determination of the feather type, but have also supplied evidence as to the nature of some of the factors conditioning the actual level of the threshold. Their experiments have shown that fast-growing feathers demand a higher concentration of female hormone than slow growing ones.[103] Thus male and female feathers may develop in a capon at the same time when the concentration of hormone is kept at a comparatively low level; but all feathers which can respond to female hormone* will assume the female type if the concentration of hormone is raised beyond a certain concentration.

There is no need to emphasize the parallel between these findings and our own deductions from observations made on mammals. In either case a difference in hormone-reactivity (determined, in birds, to some extent by the growth-rate) leads to female development in one, to male differentiation in another case, even though all controllable conditions be kept constant. Lillie has applied these findings to the theory of sex differentiation; he regards lateral hermaphroditism in birds as products of differential growth-rates of the two halves of the body; the feathers of one side may grow more slowly than those of the other side, so that, in the case of low hormone concentration, the bird would develop male plumage on one, female plumage on the other side. Such a theoretical bird would, in some measure, correspond to the actual cases described by Poll, Bond, and others.

Lillie's theory has been mentioned because the experiments on which it is based, as well as the theory itself, show that the hypothesis proffered in the preceding paragraphs with respect to mammalian genital monstrosities does not represent an interpretation without a parallel in biology. At the same time, it should be clearly realized that an explanation such as that offered by Lillie for birds and by ourselves for mammals, is possible

* i.e. which are potentially sex-dimorphic.

only when a monhormonic mechanism rules sexual differentiation.* If plumage would be sex-dimorphic in virtue of the action of two distinct and specific sex hormones, Lillie's explanation would be meaningless; one would have to explain why one side of the body reacts only to one, the other to the heteronomous hormone; in a monhormonic mechanism, of course, differences are explained by the absence or presence, or gradation, of a reaction. It will thus be recognized that our interpretation stands and falls with the conclusion expressed by

$$S = D_f$$

The rôle of reduced H_m-reactivity has been discussed, so far, only with reference to the *uterus masculinus* type of genital monstrosity. But it is obvious that it may play a rôle in the production of those abnormalities which were reduced, earlier in this analysis, to the action of a time-factor. Female external genitalia in an essentially male organism may conceivably develop, not because of a delay in the secretion of the testes, but in virtue of a relative or incapacity to react of the primordia.

The supposed reduction of H_m -reactivity is of possibly much greater significance in other cases which previously defied explanation save by rather bold auxiliary hypotheses. By these other cases we mean genital monstrosities showing lateral heteronomy of the genital characters. There is no need to give detailed descriptions of such cases; the reader is referred to the reviews of the subject.

The literature on the subject[26, 30, 31, 91, 92, 139] demonstrates the great variability of this type of genital monstrosity.[104, 105, 106, 107, 108, 109] But the general explanation is identical in all instances however much they may differ in details. We must assume that genetic or environmental factors cause a reduction in, or the complete loss of, H_m-reactivity of some, or all, primordia of one side, while reactivity is retained in the other side. Under

* A historical remark may be appended. Both in Lillie's and in our own theory, the principle of reactivity plays as great a rôle as of necessity it must in any presence-absence mechanism. The first author to realize this importance, in the writer's knowledge, was Professor M. M. Zawadowski, to whose work reference has already been made on several occasions. Zawadowski explains the lateral formation of male plumage in a female bird by the loss of reactivity. This is substantially the same idea as underlies Lillie's and Juhn's considerations. A recent American writer speaks of this explanation as purely formal and not very satisfactory. Formal it may be; fundamentally important it is, for it constitutes the first clear recognition of the rôle of reactivity in a monhormonic mechanism.

these conditions, the primordia situated on one side will undergo female differentiation even though male hormone be present. Lateral hermaphroditism will result.

It is obvious, from a reference to actual cases, that loss of H_m-reactivity may be restricted to certain primordia, for instance to the anlage of the Müllerian ducts on one side. In this case, the abnormality will be restricted to the development of a uterus on one side of the body, the other organs not being affected. Again, the loss may affect all the primordia on one side, so that a Wolffian duct will not be found on one side, but only a uterus.

We do not propose to burden this discussion with a detailed analysis of the variants of this type. If the general explanation be accepted, the reader will not find any difficulty in applying it to any specific instance.

It might be objected that the interpretation of lateral heteronomy as offered in the preceding paragraphs, does not explain how the abnormality is restricted to one side of the body. But this objection would betray confusion of thought. It is not our object to explain how asymmetry is produced; it exists, and it is for the student of "Entwickelungsmechanik" to determine the specific mechanisms which condition asymmetry. Our object is to determine the physiological nature of lateral differences, not their origin. The difference in reactivity to male hormone may be brought about by a somatic loss-mutation restricted to the parent cells of one-half of the body, or to another entirely different mechanism; this does not immediately concern the physiologist.

The principle of reduced H_m-reactivity is also applicable in a number of cases which are not strictly lateral, but represent rather disorderly mosaics. The explanation is too obvious to call for further elucidation.

It remains to refer briefly to a type of abnormality which has been referred to as virilism or pseudarrheny. The name is applied variously to cases in which development of male secondary sex characters occurs early or late in life in female subjects, when it is usually referable to the development of a suprarenal tumour. It is likely that in these cases androkinin is being secreted by the neoplastic elements, although definite evidence is not as yet available. These cases would not seem to represent an obstacle to the acceptance of the theory under discussion. However, cases have been described in the literature and referred to as female hermaphroditism and also as pseudarr-

heny or virilism, in which a penis and even a scrotum was developed although the gonads and the accessory organs were of female type. Cases of this description seem to be very rare (Neugebauer mentions only three) though another type in which masculinity is restricted to the development of the penis-like clitoris are more frequent. Goldschmidt regards all cases of this type as caused by the same mechanism which produces virilism in menopausal women; but it must be realized that evidence for this hypothesis has not been produced as yet. In the present discussion these cases are of particular interest, since, according to the theory presented here, male characters should develop only if and when androkinin is present. While the secretion of this hormone from abnormal sources cannot be excluded, and while pseudarrheny corresponds largely to the case of artificially masculinized females (see page 8), it is yet possible that other and unknown factors such as purely local, teratological changes are responsible for the development of male characters in some instances. However, no definite statement can be made at the present moment, and pseudarrheny appears to be a phenomenon which cannot readily be reconciled with the theory under discussion.

IX. Supplementary Notes.

(*a*) Critical examination of the foundation of the monhormonic theory shows that it is based, *inter alia*, on the assumption of equipotentiality of the two sexes. It may be emphasized once more that adequate quantitative data are not available which would show that the same quantity of androkinin is required to produce masculinization in the male and female respectively. The essential proposition of the theory, viz. the conclusion that female characters would develop in either sex in the absence of male hormone, would not be impaired should it be shown that male and female exhibit differential reactivity to androkinin; but less essential qualifications would obviously become necessary.

(*b*) The findings described in Section VI also indicate a possible way of testing the validity of the theory. It has been shown that ketohydroxy-oestrin when administered in comparatively large doses produces anti-orchidic effects. The administration of large quantities of ketohydroxy-oestrin to undifferentiated rat embryos should result in the suppression, partial or complete, of testicular secretion and in the production of individuals of predominantly or entirely female character.

(*c*) It will have been noted that the theoretical discussion offered in the preceding section omits any reference to the mechanism which determines the differentiation of the gonad. The existence of either male or female gonad has been assumed and reference to gonadic structure has not been made. However, genital abnormalities are not infrequently combined with gonadic abnormalities, and lateral heteronomy in particular may not be restricted to the accessory organs, but also involve the gonads, so that an ovary may be found on the side which is predominantly female, while a testis is present on the predominantly male side. This restriction of the discussion was necessary because new data regarding the gonad have not been ascertained. It should be mentioned, however, in this context that the gonad might conceivably behave like an accessory genital, i.e. the testis might require for its proper formation the presence of testicular hormone secreted by certain of its constituents,* whereas the ovary would not require any such hormone or rather only intracellular factors. This point of view would seem to receive a certain support from the fact that the gonad is, in many free-martins, very obviously influenced and resembles a testicle rather than an ovary. Absence of reactivity to testicular hormone might condition the appearance of an ovary in a genetic male; partial absence of reactivity the appearance of an ovo-testis. While these considerations are purely speculative, it should also be mentioned that Witschi[2] has advocated a theory which involves the view that the structure of the gonad is determined by one of two organizators, one represented by the medulla, the other by the cortex of the primordium.

(*d*) The theory under discussion has been derived from experiments on, and is proposed only for, mammals. It might be objected that monhormonic mechanisms have not been demonstrated for other vertebrates with the exception of birds, in which they seem to be restricted, as far as our knowledge goes, to the development of the plumage. Methodically, however, this objection would not deserve consideration. Moreover, where dihormonic mechanisms of sexual differentiation are assumed, the facts do not really seem to be convincing. As to experiments on parabiosis in amphibia,[2] it has been found that in the great majority of cases the male is dominant insomuch as it imposes transformation upon the female gonad. As to the

* i.e. interstitial cells or their forerunners; these secretory elements might be active before testicular structure becomes manifest. For literature, see Stieve, Kolmer, *et al.*

rare cases in which the converse relation obtained (suppression of male differentiation), it was observed that in the genetic male, the development of the gonadic medulla was delayed; thus the further development of the gonad would proceed under the influence of the cortex. It is conceivable that delayed male development permitted the ovary to secrete hormones of anti-orchidic action, such as has been demonstrated for oestrin; moreover, Witschi states that "female induction is successful only in those parts that lie closest to the ovaries of the female and that this limited effect is of short duration, since in the further development the male again assumes the leading rôle."*

(*e*) According to Goldschmidt's theory of intersexuality certain types of genital abnormality are regarded as mosaics in time. It is assumed that a primordium may develop up to a certain point in one direction, continuing thereafter its development in the heterologous direction; one kind of determining hormone is assumed to control development for its first period, when the heteronomous hormones assumes control. At any given moment any organ is, therefore, developing in either male or female direction. No simultaneous mixture is assumed to occur.[54]

If this theory is analysed with respect to its basic propositions it is found that its general validity stands and falls with two assumptions—(I) and (II).

(I)

It is implied that male and female development follow the all-or-nothing law; that is to say, the substances (intracellular or extracellular) which determine either reaction must exert a full effect or none at all if only male or female development is to result. Goldschmidt is aware that the theory of intersexuality implies the assumption but refers to it only in one instance† (*Physiologische Theorie der Vererbung*, pp. 37–38) where he

* The hypothesis that the male structure of the gonadic free-martin depends on male hormone, whereas the formation of ovarian structure is not dependent on extra-cellular hormones would seem to give added interest to experiments carried out by Woronzowa and Blacher, who found that double hypophysectomy performed in hetero-sexual parabiotized amphibian twins arrests the further development of the testis and is followed by restoration of the free-martin's gonad, which assumes ovarian character. The activity of either gonad appears to depend on pituitary factors, but secretion of extra-cellular hormones may not be necessary for the formation of an ovary.

† As far as the present writer is aware.

says: "Im gleichen Individuum haben also bestimmte Entwickelungsvorgänge, z.B. die Wachstumsprozesse der Abdominalsegmente, die zur Ausbildung des Kopulationsapparates führen, oder die Differenzierungsvorgänge der Urgeschlechtszellen, eine Alternative (männlicher oder weiblicher Typus) zur Wahl, zwischen der es keinen Uebergang giebt (das Alles- oder Nichtsgesetz!)"

It seems that this proposition is by no means generally valid. In the first instance, the all-or-nothing law has not been established with respect to any activity depending on hormones (see p. 58). In the present communication it has been shown, for instance, that the effects of androkinin upon the clitoris can vary in intensity, and many other examples of graded action will be found in the literature.

Quantitatively differing effects may not only be represented by varying degrees of stimulation but also by variation in the suppression of development or the supersession of anhormonic development. For actual instances one may refer to the transformation of the male into a female feather—this can be graded at will; or the incomplete involution of the Müllerian duct.

(II)

It is assumed, in the theory of intersexuality that male and female differentiation of any given primordium are superimposed upon a common (basic) form. Female differentiation would represent the development of this basic form in one direction, male differentiation in the other. If, however, the female type is identical with the basic type an actual "Misch-Charakter" (such as should not exist according to that theory) must result whenever the male determiner is insufficient to impress fully male characters upon the gonad primordium (or vice versa).

Reference to the clitoris may be made once more. Here enlargement and partial transformation may occur, and while this partial change is effected the organ does not develop in full male direction, nor does it pursue undisturbed female differentiation. Similar instances are provided by the behaviour of feathers.*

It appears, therefore, that the sharp definition of intersexuality cannot be reconciled with facts established since the theory was propounded.

(*f*) Lastly, the variations in reactivity and the possible exis-

* It is possible that further investigation of these true "Mischcharaktere" will necessitate a revision of terminology.

tence of local irreactivity (such as has been demonstrated for some regions of the plumage in certain breeds of the domestic fowl) may require the recognition of a new type of genital heteronomy. It is appropriate to choose the fowl as an instance. A female bird displaying male feathers, say, in the saddle region (where the producing follicles do not react to oestrin) would not be regarded as abnormal if all birds of that particular breed showed the same constitution.

But if the local irreactivity to oestrin were abnormal it could not be placed in any category recognized by Goldschmidt or the other workers who followed in his footsteps.

Obviously, the bird could not easily be regarded as gynandromorphic unless definite reactions would suggest abnormality in the distribution of sex chromosomes. Nor could it be regarded as an intersex, the time-factor being absent (i.e. even if the feather were removed and permitted to be replaced under definitely female hormonic conditions it would exhibit male type). In other words, genital heteronomy based on local reactions represents neither intersexuality nor gynandromorphy. Should it become necessary to use a specific expression for this type the term "Hybristicism"* might be used.

* See Plutarch; *Lyc.* xv; ibid. *Mor.* 304.

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Description of Plates.

PLATE I.

Fig. 1. Glans penis of newborn male; sheath removed but part of the parietal lining still adherent to glans.

Fig. 2. Glans penis of intact male aged 14 days. Note anterior process.

Fig. 3. Glans penis of intact male killed at completion of maturation (aged 85 days). Preputial folds not wholly removed.

Fig. 4. Glans penis of male castrated when 0.5 days old. Killed aged 17 days. Note absence of process.

Fig. 5. Glans penis of male castrated when 0.5 days old. Killed aged 37 days.

Fig. 6. Glans penis of male castrated when 0.5 days old. Killed aged 240 days.

Fig. 7. Seminal vesicles (sv) of newborn male. Note distal portions of *vasa deferentia* (sd) on either side of vesicles. Bladder removed.

Fig. 8. Seminal vesicles of intact male aged 21 days.

Fig. 9. Seminal vesicles of male castrated when 0.5 days old. Killed aged 21 days.

Fig. 1–9: magn. 5×

Fig. 10. Cross-section through glans penis (median region) of newborn male. (i) Integumen of glans sectioned *in situ* within the dermal sac. (10×).

Fig. 11. Cross-section through anterior region of glans penis of intact

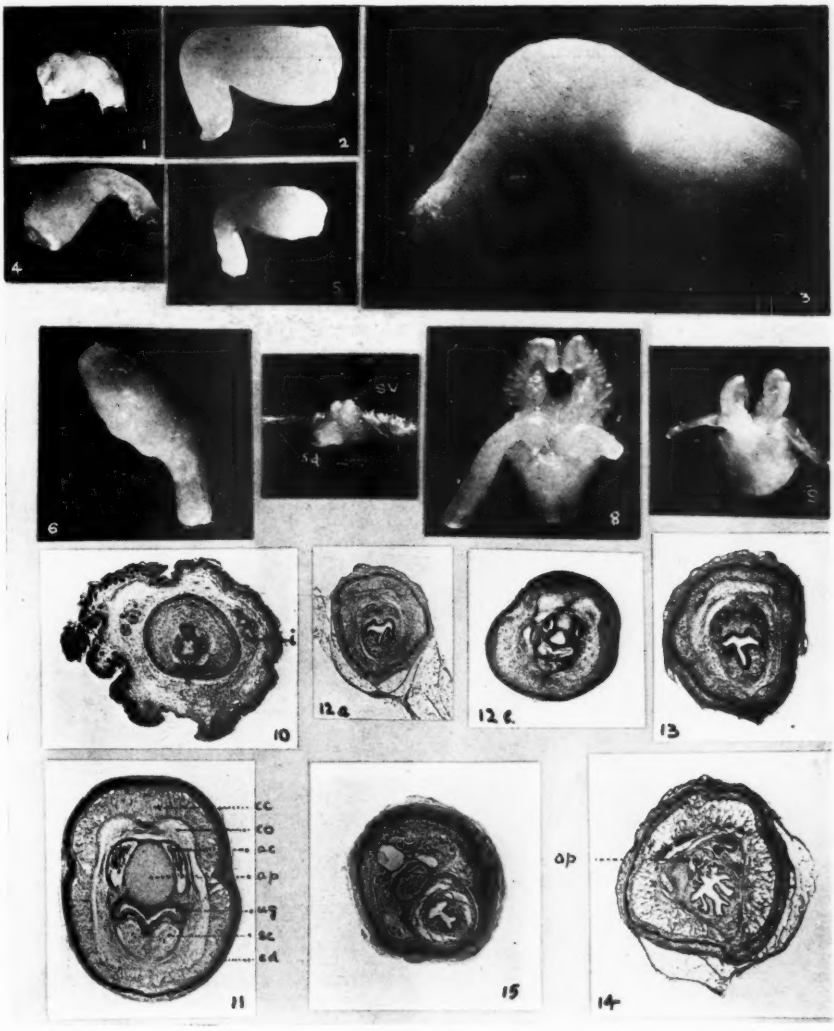

PLATE I.

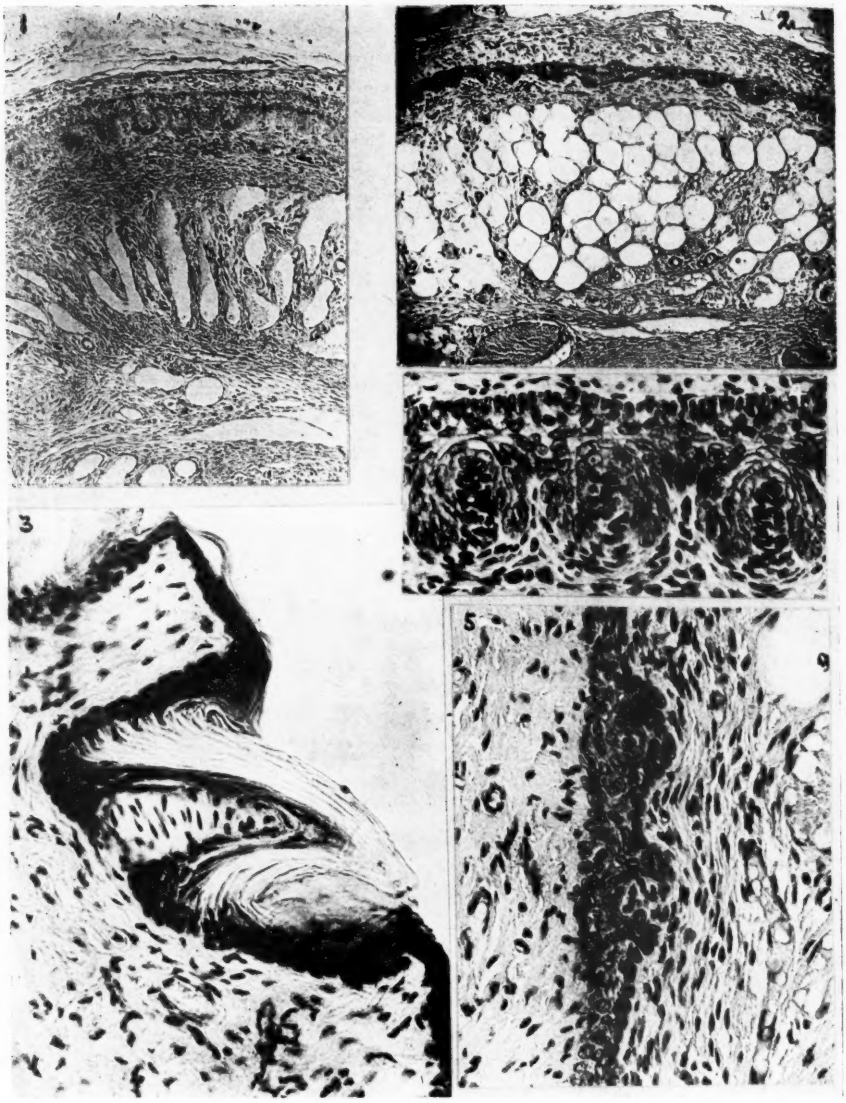

PLATE II.

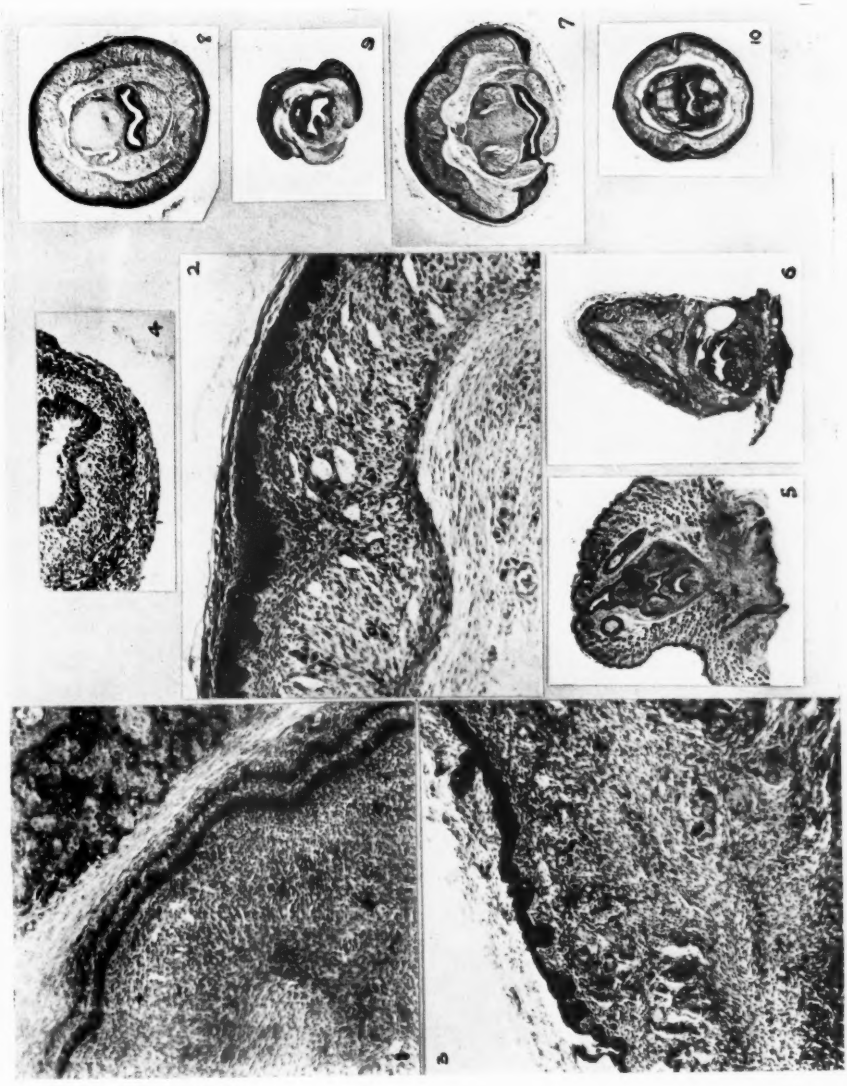

PLATE III.

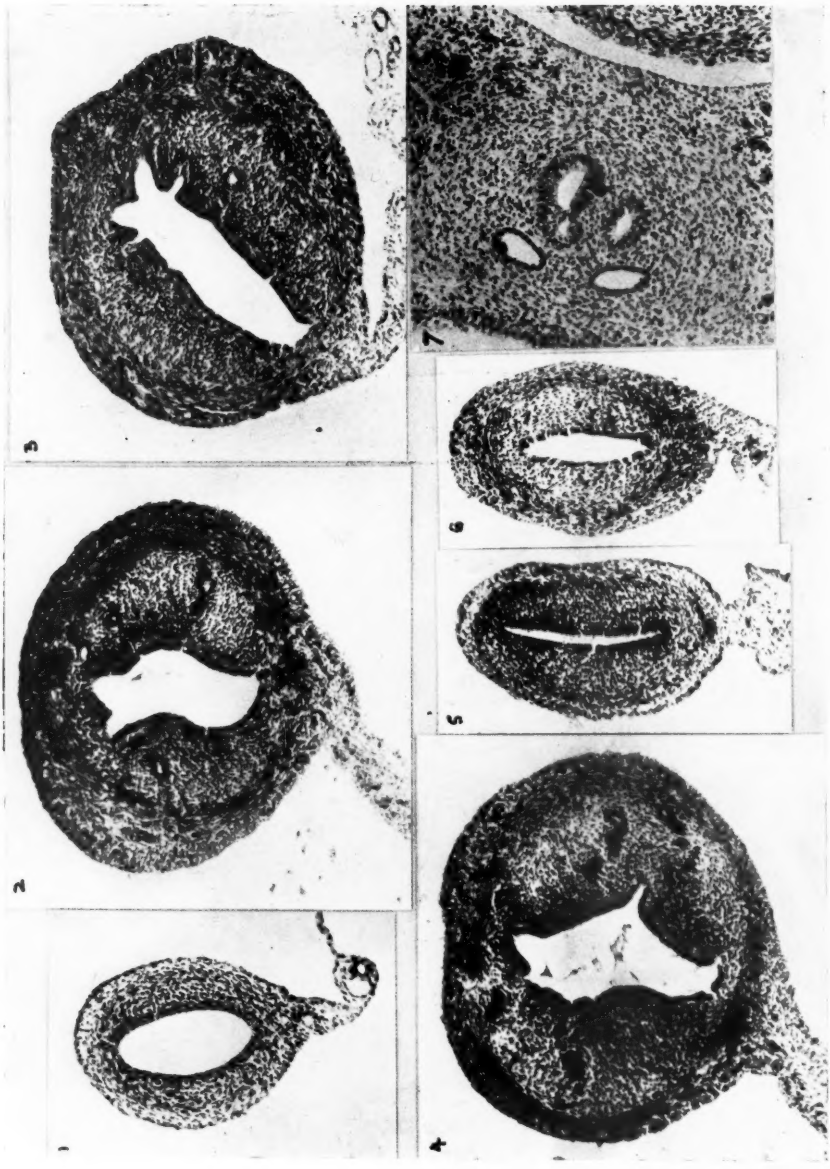

PLATE IV.

male aged 14 days. (*c c*) corpus cavernosum glandis penis; (*c o*) connective tissue between *c c* and inner structures; (*a c*) accessory cavernae; (*a p*) anterior process; (*u g*) urogenital sinus; (*s c*) cavernous tissue accompanying the urogenital sinus ("corpus cavernosum urethrae"); (*e d*) epithelial lining of dermal sac. (15×).

FIG. 12 (*a*). Cross-section through anterior region of glans penis of male castrated when 0.5 days old. Killed aged 21 days. (*b*) Cross-section through glans penis (region of anterior end of os priapi) of male seven days old. (10×).

FIG. 13. Cross-section through anterior region of glans penis of male castrated when 0.5 days old, killed aged 28 days. (10×).

FIG. 14. Cross-section through median region of glans penis of male castrated when 0.5 days old. Killed aged 84 days. (*o p*) os priapi. (15×).

FIG. 15. Cross-section through posterior (proximal) region of glans penis of male castrated when 0.5 days old. Killed aged 21 days. (15×).

PLATE II

FIG. 1. Corpus cavernosum and integument of glans penis of intact male, aged 21 days.

FIG. 2. Corpus cavernosum and integument of median region of glans penis of male castrated when newborn; killed aged 21 days.

FIG. 3. Papilla from the integument of the glans penis of mature male (aged 85 days). The "thorns" are curved; thus no plane section can be laid through the whole "thorn" from apex to base.

FIG. 4. Anlagen of papillae (glans penis of intact male aged 21 days).

FIG. 5. Undeveloped and partially de-differentiated papillae of castrate; same specimen as in Fig. 2.

PLATE III

FIG. 1. Median region of clitoris; part of corpus glandis, integument and sheath. Intact female 21 days old. (100×).

FIG. 2. Median region of clitoris; female injected with proviron, 21 days old. (100×).

FIG. 3. Median region of clitoris (slightly nearer apex than 1 and 2. Mature intact female. (100×).

FIG. 4. Vaginal wall and epithelium; female four days old; 600 units of menformon. (100×).

FIG. 5. Clitoris; intact female three weeks old. (15×).

FIG. 6. Clitoris; mature female; intact. (15×).

FIG. 7. Clitoris; female injected with proviron; three weeks old. (15×)

FIG. 8. Penis; male injected with ketohydroxy-oestrin and proviron (15×). Section through distal end of os priapi; the latter is seen embedded in the cartilage. (15×).

FIG. 9. Penis; male injected with ketohydroxy-oestrin (15×). Sectioned as (8). (15×).

FIG. 10. Penis; castrate injected with proviron (15×). Sectioned as (8) and (9). (15×).

PLATE IV

FIG. 1. Uterus of female, 0.5 days old. Specimen shows most advanced development observed.

FIG. 2. Uterus, intact female, 21 days old.

FIG. 3. Uterus, oöphorectomized female, 21 days old.

FIG. 4. As (3); different specimen.

FIG. 5. Uterus; intact female four days old.

FIG. 6. Uterus, injected female, four days old (600 units menformon).

FIG. 7. Section through Müllerian duct; female sheep embryo.

All specimens 100×

Studies on the Movements of the Uterus

BY

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II. THE ACTION OF EXTRACT OF CORPUS LUTEUM ON THE UTERUS OF THE UNANAESTHETIZED RABBIT.

IN a previous communication to this journal[1] I have described experiments which suggest that the motor activity of the uterus of the unanaesthetized non-pregnant rabbit depends upon variations in the quantity and nature of the ovarian hormones in the circulation. In particular, I have corroborated Reynolds's observation,[2] that coitus in the female rabbit is followed by a period of inactivity of the uterus, which lasts throughout pregnancy. The onset of this quiescence 24 hours after coitus corresponds in time with the formation of corpora lutea in the ovaries, a fact which suggests that the internal secretion of this tissue is responsible for the inhibition of uterine movement seen during pregnancy.

Further evidence bearing on the inhibiting effect of the corpus luteum on uterine muscle has been provided by Keye,[3] who tested *in vitro* the activity of strips of uterine muscle of the sow, removed at different stages of the sexual cycle, and found that strips removed during pregnancy remained quiescent. Knaus,[4] experimenting on the rabbit's uterus *in vitro*, has reported similar results. More recently, Reynolds,[5] using unanaesthetized rabbits with uterine fistulae prepared by transection of the vagina, has shown that active extracts of corpora lutea are capable of inducing quiescence of the uterus and of inhibiting the effect of oestrin in causing increased uterine activity.

In the following experiments, the action of corpus luteum extracts on the movements of the uterus of the unanaesthetized rabbit was investigated, and the effects obtained correlated with changes induced in the structure of the uterus by the luteal hormone.

The method of preparing the fistulae used in these experiments has been previously described in full.[1] One horn of the uterus is

isolated from the vagina and fixed to the abdominal wall so as to be available for providing records of the movements of the organ, the other being left *in situ*, and from it tissue can be obtained for histological examination.

Two groups of animals were used, one group consisting of immature animals and the other of sexually mature does, the histories of which, with regard to previous pregnancies, were known. All the animals were isolated for at least three weeks prior to experiment.

The luteal extract employed was a commercial preparation of sow's corpora lutea, issued under the name of "prolution" by Schering Kahlbaum, A.G. (I am indebted to Dr. Strauss of Berlin for a generous supply of this material.) Before use, each batch was tested for its activity in producing pseudo-pregnant development of the rabbit's endometrium. (Corner and Allen.)

Group I.

Uterine fistulae were prepared in sexually immature animals, and at the same operation a piece of uterine tissue was removed for histological examination. A few days were allowed for recovery, and records of uterine movement were then made. In the infantile animal the uterus is very small, and the contractions registered are of necessity slight. (Figs. 1 and 2.)

The animals were then injected with 20 mouse-units of oestrin daily for six or seven days, records of uterine activity being made periodically throughout the period of injection. At the end of that time it was found that the contractions of the uterus had greatly increased in magnitude (Fig. 3.) The abdomen was again opened and a piece of uterine tissue excised and examined histologically. It was found that the uterus was increased to more than twice its original size, and its endometrium showed the typical oestrous development. (Fig. 4.)

The oestrin injections were now discontinued and injections of relatively large doses of corpus luteum extract substituted, 10 clinical units (3 rabbit-units) being administered daily. Records of the movements of the uterus were made each day, and it was found that the activity of the uterus diminished within 48 hours of commencing the injections; by the end of three days' treatment the record was indistinguishable from that obtained during pseudo-pregnancy (Fig. 5). A biopsy was performed after four to five days, when uterine inactivity was well established, and histological examination of the material obtained showed full pseudo-pregnant proliferation of the endometrium. In addition,

FIG. 1.
Section of the uterus of an infantile rabbit.

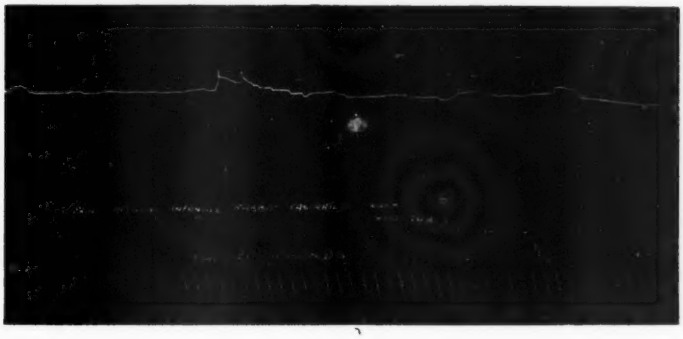

FIG. 2.
The movements of the uterus of the animal from which the specimen in Fig. 1 was taken.

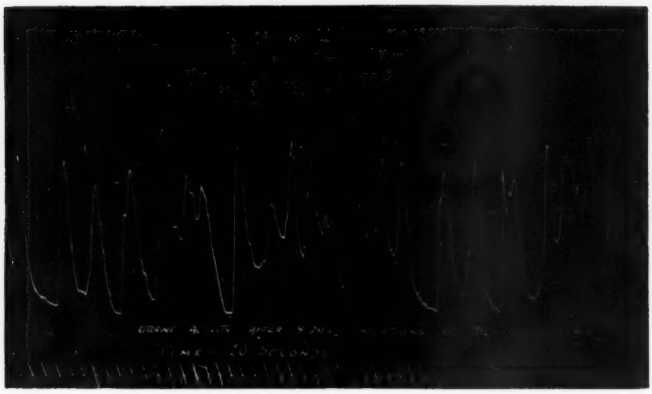

FIG. 3.

The movements of the uterus of the same animal after eight daily injections of 20 mouse-units of oestrin.

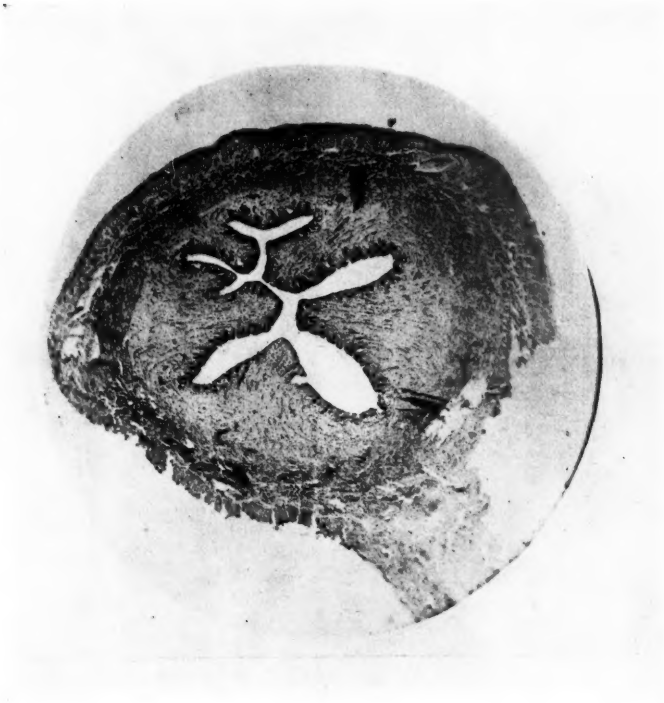

FIG. 4.

Photomicrograph showing the structure of the uterus after oestrin treatment.

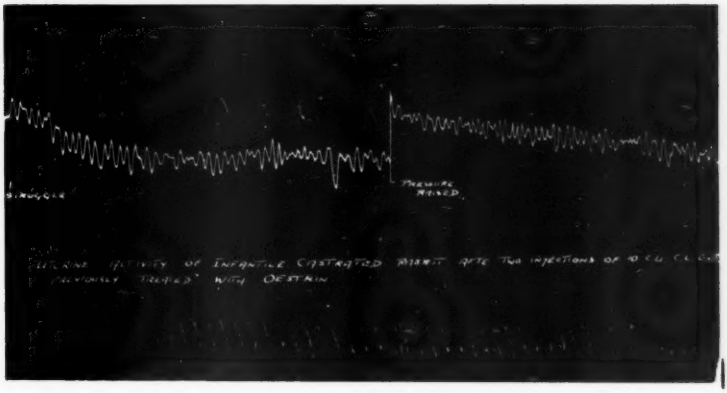

FIG. 5.

The movements of the uterus of the same animal after two daily injections of 10 clinical units of corpus luteum extract.

FIG. 6.

Photomicrograph of a section of the uterus, removed four days after commencing corpus luteum injections, showing endometrial proliferation.

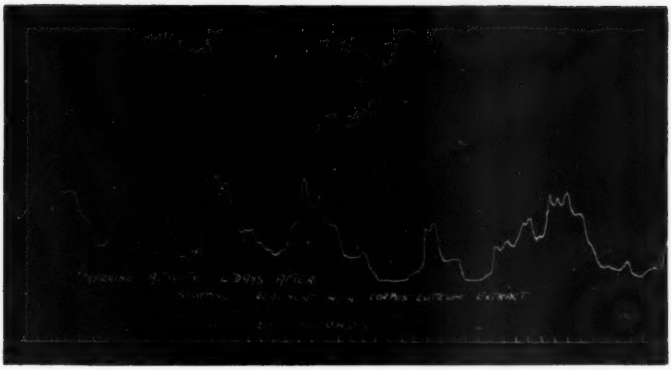

FIG. 7.

The movements of the uterus recorded four days after stopping treatment with corpus luteum extract.

FIG. 8.

Photomicrograph of a section of the uterus removed four days after stopping corpus luteum treatment; showing loss of endometrial proliferation.

it was observed that the uterus had increased in size during the course of the corpus luteum treatment (Fig. 6). When this result had been obtained, the corpus luteum injections were stopped and records of uterine movements made daily in order to observe the duration of the effect. It was found that the uterus gradually became active again, the earliest sign of returning activity being seen usually three days after the cessation of the injections (Fig. 7). A piece of uterine tissue removed at this time showed regression of the endometrium, with loss of the endometrial proliferation (Fig. 8).

Similar experiments were performed on sexually immature animals in which the ovaries had been removed and identical results were obtained.

From these results it would appear that the hormone of the corpus luteum is capable of inhibiting uterine movements in the unanaesthetized animal. It is, however, possible that the diminished activity of the uterus may have resulted from the cessation of oestrin injections. The close similarity between the type of movement obtained under corpus luteum treatment and that seen during normal pseudo-pregnancy, together with the fact that the cessation of corpus luteum treatment initiated a return of uterine activity much greater in degree than was seen before the injections of ovarian hormones were begun, suggest strongly that the corpus luteum hormone was responsible for the inhibiting effect.

Group II.

The action of extract of corpus luteum was next tested on the group of sexually mature rabbits, both on animals in which the ovaries had been removed and on animals with intact ovaries.

The effect produced on the uterine movements of the castrated group of animals was substantially similar to that seen in infantile animals. It has been previously demonstrated[1] that oöphorectomy in the sexually mature female rabbit does not cause cessation of uterine movement but that the uterine contractions become infrequent and regular and show only slight diminution in amplitude. Animals in which this type of uterine activity had been induced by oöphorectomy were treated as in the previous experiments with a course of injections of oestrin, 20 units being given daily for five days. At the end of that time the activity of the uterus was very much increased, and the animals were then injected daily with 3 rabbit-units of corpus luteum extract. As in the previous experiments, it was found that within 48 hours of commencing the injections, the activity of the uterus had

diminished, and the records finally obtained were similar in every way to those obtained from normal pseudo-pregnant animals. Sections of the uterus examined after four or five days of corpus luteum treatment showed the structural changes typical of pseudo-pregnancy.

In several experiments in this group, initial treatment with oestrin was omitted, and in these animals it was found that corpus luteum extract administered in similar doses was ineffective both in inducing uterine quiescence and in altering the structure of the uterus.

The effect of the luteal extract on the uterine activity of mature rabbits the ovaries of which remained intact, was not constant. The animals were treated as before with injections of oestrin followed by corpus luteum extract, and it was found that while in some cases the uterine activity remained unaffected by the corpus luteum injections, other animals showed some diminution in uterine activity, which was, however, never so marked as in the previous experiments on castrated and on infantile animals; the uterus never reached the degree of quiescence usual for pseudo-pregnancy. Histological examination of the uteri of animals in which uterine activity persisted in spite of corpus luteum treatment, did not show any structural alteration, while examination of uteri which had become somewhat diminished in activity showed at most a commencing corpus luteum effect.

Experiments were performed in which the dose of corpus luteum extract was increased to 4 rabbit-units daily, but similar results were obtained. These findings are in accordance with those of Allen[6] and of Clauberg,[7] who have shown that a synergistic relation exists between the follicular hormone and the hormone of the corpus luteum, in that the corpus luteum hormone is unable to produce the structural changes of pseudo-pregnancy in the uterus unless the uterus is first acted on by oestrin. Leonard, Fevold, and Hisaw[8] have carried out careful quantitative experiments and have demonstrated that in addition to this synergism there exists also an antagonism between the two hormones, in that the effect produced upon the uterine endometrium by the simultaneous administration of oestrin and corpus luteum hormone depends upon the relative amount of each hormone in the circulation, since large doses of oestrin may annul the effect of smaller amounts of corpus luteum hormone. It must be assumed, therefore, that in the above experiments, the amount of corpus luteum extract administered was insufficient to counteract the effect of endogenous oestrin.

SUMMARY.

From the foregoing experiments it is concluded that an active extract of corpus luteum, injected into suitably prepared sexually immature rabbits, whether castrated or with intact ovaries, is capable of inducing quiescence of the uterus identical with that which is associated with the presence of normal corpora lutea in the ovaries.

The action of corpus luteum extract on the movements of the uteri of sexually mature rabbits is, however, profoundly affected by the presence or absence of the ovaries. In animals in which the ovaries have been removed, treatment with corpus luteum extract inhibits the contractions of the uterus, while in animals with intact ovaries, the luteal hormone is almost without effect in altering the activity of the uterus or the structure of the endometrium. It would seem, therefore, that the follicular hormone and the corpus luteum hormone exercise respectively augmentor and inhibitor effects on the motility of uterine muscle, and that the degree of activity of the uterus depends on the relative concentrations of these hormones in the blood. This fact should be kept in mind in cases in which corpus luteum extract is to be employed in human therapeutics. For while relatively small doses of this hormone may be effective in inducing endometrial transformation in cases in which the ovaries are absent (Kaufmann[9]), it is likely that very much larger doses may have to be employed in order to produce effects in cases in which the ovaries are intact and secreting oestrin into the circulation.

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III. The Action of Gonadotropic Extracts on the Movements of the Uterus of the Unanaesthetized Rabbit.

In a previous communication to this journal,[1] some observations on the action of a saline extract of anterior pituitary gland on the movements of the uterus have been reported, and the present communication records the results of further experiments with this hormone. Fistulae were prepared in various ways in a series of rabbits, and the action of gonadotropic extracts on the movements of the uterus was tested on animals with intact ovaries and on animals in which the ovaries had been removed. Extracts of urine secreted during pregnancy in solution issued by Parke, Davis & Co. under the name of antuitrin S, a similar dried extract, pregnyl, issued by the Organon Co., and saline extracts of anterior pituitary ox gland obtained from Armour & Co. were used. Identical results were obtained with all three preparations, but it was found that both the antuitrin S and the anterior pituitary extract tended to lose potency rapidly on keeping, and this introduced a difficulty in correlating ovarian changes with the dose of gonadotropic substance administered. The dried extract, pregnyl, was, however, more satisfactory, its activity remaining uniform for longer periods.

In the first set of experiments, animals in which fistulae had been prepared and in which the ovaries remained intact were injected with various doses of an extract of urine secreted during pregnancy, and frequent records of the movements of the uterus were made. When any significant change occurred in the activity of the uterus, laparotomy was performed and the ovaries were inspected.

In this way it was found that when animals showing marked initial activity of the uterus were injected subcutaneously, or intravenously, with large doses (50 to 75 rat-units) of gonadotropic extract, the uterus became inactive within two or three days, and remained in this state for varying periods up to three weeks (Figs. 1*a* and 1*b*). Laparotomies were performed when inactivity was established and the ovaries were found to show corpora lutea and blood-filled follicles. As a control experiment, several animals were first injected with similar doses of an extract which had been previously boiled to destroy gonadotropic activity. The injection of this extract had no effect in altering either the

Description of Plates.

Fig. 1.

A. Tracing of the movements of the uterus of a sexually mature doe before treatment.

B. The movements of the uterus of the same animal 60 hours after the intravenous injection of 75 rat-units of an extract of urine excreted during pregnancy.

C. The contraction of the uterus of the same animal 24 hours after the removal of both ovaries. (Note the increased size of the contractions.)

Fig. 2.

Uterine movements of a young virgin doe during treatment with repeated small doses of gonadotropic substance.

A. Before treatment.

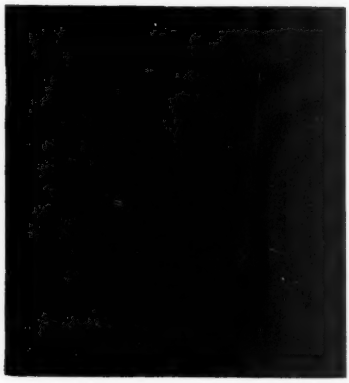
B. Thirty-six hours after the intravenous injection of 3 rat-units of an extract of urine excreted during pregnancy.

C. Twenty-four hours after a second injection of 3 rat-units of an extract of urine excreted during pregnancy. (Note the increase in the size of the contractions.)

The animal was allowed to remain without further treatment for three days, during which time the activity of the uterus was maintained. The animal then received an injection of 6 rat-units of an extract of urine excreted during pregnancy; and D shows the activity of the uterus 48 hours after this injection.

E shows the activity 60 hours later. The activity of the uterus is similar in every way to that seen during pseudo-pregnancy.

FIG. 1.



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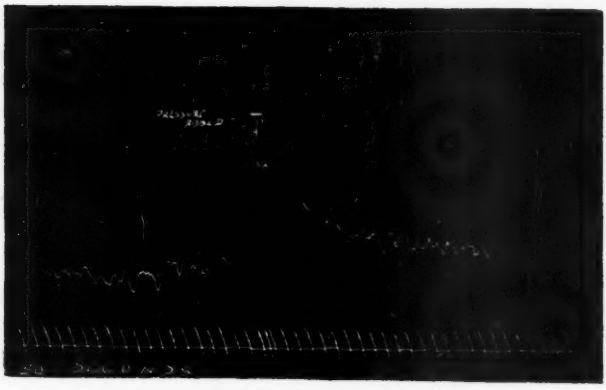

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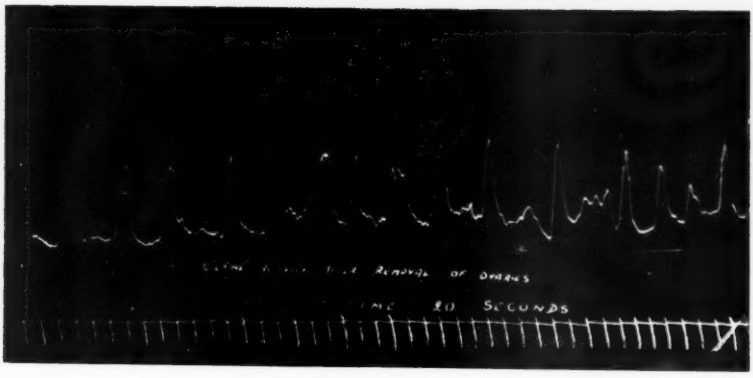

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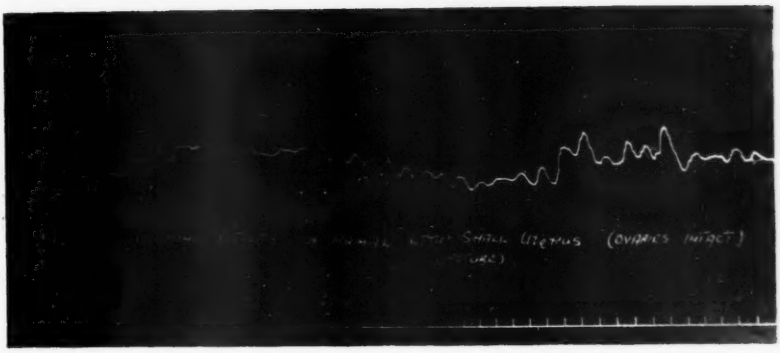
FIG. 2.



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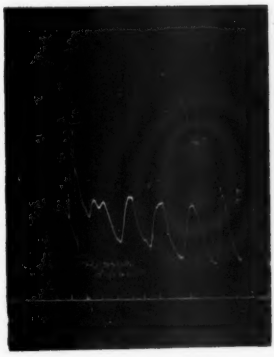

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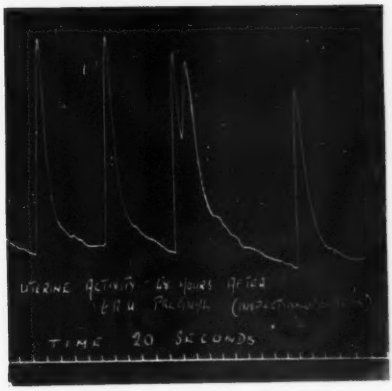

C

D

E

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activity of the uterus or the structure of the ovary. The animals were then treated with an unboiled extract and, as before, the activity of the uterus diminished within 48 hours, while subsequent inspection of the ovaries showed the presence of recently formed corpora lutea and "Blut Punkte". That the change in the motility of the uterus depends upon the formation of corpora lutea in the ovaries is shown by the fact that in these experiments removal of the ovaries when uterine inactivity is established is followed by an increase in uterine activity within 24 hours (Fig. 1*c*).

To determine the effect on the movements of the uterus of small doses of gonadotropic substance, intact animals showing relative inactivity of the uterus were injected with 12 to 16 rat-units of gonadotropic extract in divided doses, 3 rat-units being given daily. It was found that the uteri of these animals within 48 to 60 hours showed an increase in activity which lasted for many days. When the movements of the uterus showed a marked increase, the ovaries were inspected and the follicles were found to be enlarged without evidence of corpus luteum formation.

These experiments demonstrate that it is possible, by giving small doses of gonadotropic substance, to produce follicle ripening without ovulation and corpus luteum formation. In two of six animals examined in this way, however, the uterus after first becoming active became inactive again within a day or two, and laparotomy at this time showed corpora lutea in the process of formation. In these animals the gonadotropic substance had induced ovulation, and the ruptured follicles had formed corpora lutea.

To determine whether it was possible to simulate the natural occurrence of sexual maturity by the administration of gradually increasing doses of gonadotropic substance, immature animals were injected with repeated small doses of gonadotropic extract. Records of uterine activity were made and the ovaries inspected at intervals in the course of the injections. It was found that by injecting small daily doses of gonadotropic substance the contractions of the uterus could be markedly increased in size. When this increased activity was well established, the injections were stopped and the behaviour of the uterus observed over several days; when spontaneous diminution in activity did not occur, the injections were recommenced and the dose increased to 6 rat-units daily. Forty-eight hours after one such dose the movements of the uterus were diminished in amplitude, and 60 hours later the type of record obtained was similar in every respect to that obtained

during pseudo-pregnancy (Fig. 2), while the ovaries showed signs of recent ovulations and early corpus luteum formation.

From these experiments it is clear that the gonadotropic substance in the urine during pregnancy, or anterior pituitary extract, has a profound influence on the motor activity of the uterus, but they suggest that it exerts its influence through the ovary.

To determine whether there was any substance in the extract capable of affecting uterine muscle directly, animals with fistulae, in which the ovaries had been removed, were injected with doses of an extract of urine from pregnant women varying between 6 and 100 rat-units.

Records made at two-hourly intervals after the injections did not show any alteration in uterine activity that could in any way result from the injections. The experiments were repeated on animals in which the ovaries had been removed and which had been previously treated with oestrin, but diminution in uterine activity was not observed in these animals. The observation reported by Reynolds[2] that gonadotropic extract is capable of inducing a transient period of uterine quiescence in animals in which the ovaries had been removed and which have been previously injected with oestrin, has thus not been confirmed. Similarly, the treatment of spasmodic dysmenorrhoea with gonadotropic extract, as advocated by Novak and Reynolds,[3] would appear to be without the support of animal experiment.

Conclusions.

It is concluded that the effect of gonadotropic extracts on uterine motility depends upon the effect produced on the ovary by the extract. If follicular enlargement occurs, the uterus shows an enhanced degree of activity, whereas if ovulation occurs and corpora lutea are formed, the movements of the uterus diminish, to become of the type seen during pseudo-pregnancy. Which of these effects predominates depends upon the dose of extract administered. Thus small doses lead to follicular enlargement, with increased production of oestrin and increased activity, while large doses lead to luteinization of the ovary and uterine quiescence. By suitable dosage, the uterus of a young animal can be made to pass through various phases of activity, depending upon the functional condition induced in the ovaries.

Neither extracts of urine secreted during pregnancy nor anterior pituitary extract has any effect on the movements of the uterus of castrated animals.

I wish to express my thanks to Professor David Campbell for the help he has provided in the performance of the above experiments and for his constant interest and encouragement. To Mr. J. R. Campbell I owe my thanks for valuable technical assistance.

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Menstruation and Menstrual Disorders

BY

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TO-DAY it is regarded as an axiom that functional uterine bleedings, so interesting to the gynaecologist, are due to a disturbance of the endocrine balance which maintains the normal menstrual cycle. It is impossible, therefore, to appreciate the proper significance of these pathological bleedings unless we are well grounded in the physiology of menstruation. Since fresh discoveries are constantly being made in this fascinating field of study, it is necessary that we should revise from time to time our conceptions in regard to the nature and cause of functional uterine bleedings in the light of the most recent advances in the physiology of menstruation.

In the interpretation of the menstrual cycle two separate but closely related problems can be distinguished. The first concerns the physiological determinants of menstrual bleeding, and the second the relation between the rhythmical phases of the menstrual cycle and those of the sexual cycle in the lower animals.

PHYSIOLOGY OF MENSTRUATION.

Until recently it was generally assumed that the withdrawal of the ovarian hormones is an adequate cause of menstrual bleeding. Some clinicians, notably Novak,[1] still adhere to the traditional view. In reference to the passive or negative theory of menstruation, as it is called, I quote a passage from a paper which I contributed to the *Irish Journal of Medical Science* in 1930:

> "That the endometrial edifice which has been built up under the influence of the ovarian hormones should collapse without their support is something I can readily understand: that the endometrium, however, should shed blood on

account of this loss is too much for my credence. I prefer to think that a hormone, toxin—call it what you will—probably manufactured outside the ovary is the active cause of menstruation."

In strict logic, a negative cause is a meaningless expression. By "cause," in the strict philosophic sense, we mean that which produces an effect or "something new" by some positive influence. We must distinguish the cause, in the sense defined, from the conditions, positive or negative, under which it operates. The conditions are discovered by the same principles of inductive logic as the cause itself, and, from the practical point of view, are just as important. In the empirical sciences, therefore, our ideal should be to discover the conditions, as well as the cause, of the "something new" we are investigating. Now the withdrawal of hormonic support may be a negative condition of menstrual bleeding. It cannot, in strict logic, be the cause.

Frankl's View of the Mechanism of Bleeding.

Although Frankl's view is no longer accepted, he was the first to have formulated a theory of menstruation which satisfies the demands of the category of causality, including as it does not only the actual cause, but also the conditions, positive and negative, of menstrual bleeding. According to Frankl,[2] the corpus luteum elaborates a special hormone which is responsible for the secretory phase of the human menstrual cycle. This phase is characterized by the presence of mucus in the large tortuous glands, and of oedema and hyperaemia of the stroma (the positive condition). On the death of the ovum, the corpus luteum begins to degenerate, and the turgescence of the endometrium subsides. The efferent ducts, which have been closed by the oedematous endometrium, are now open, and so mucus escapes into the cavity of the uterus (the negative condition). The mucus which contains trypsin (the actual cause) digests the vascular endometrium. Hence the flow of menstrual blood. In other communications[3] I have criticized Frankl's theory at some considerable length. Here it is sufficient to say that his theory, although it meets the requirements of the category of causality, completely breaks down in the attempt to explain non-ovular menstruation in which the secretory phase is characteristically absent.

Human beings, the apes and the old-world monkeys, are the only animals that menstruate in the strict sense of the

word. It is remarkable that these are the only forms which have a peculiarly haemorrhagic implantation. A study of the parallelism between the haemorrhage of menstruation and that of implantation has led Hartman to abandon the passive or negative view in favour of a positive cause of menstrual bleeding. Hartmann[4] carried out a series of experiments to locate the source of the blood-producing factor. It is well known that the administration of oestrin to the castrated monkey provokes bleeding as soon as the injection is discontinued. According to Hartmann, the bleeding is prevented by removing the pituitary gland of the castrated monkey. Therefore he suggests that the pituitary body, in addition to the sex hormones (prolan A and prolan B), contains a bleeding factor which is the active cause of menstruation.

The production of bleeding[5] by the administration of anterior pituitary extract to the non-castrated monkey from which the pituitary gland has been removed established the theory.

Many criticisms have been levelled against Hartmann's experimental results and their interpretation. It was found by Saiki[6] that bleeding does not follow the administration of anterior pituitary extract to the castrated monkey from which the pituitary gland has been removed. According to Saiki, therefore, the crucial test fails when carried out under strict experimental conditions. In my opinion the inference is not logical. It is one of the fundamental principles of endocrinology that not only are certain tissues of the body sensitive to the stimulus of a particular hormone, but the same tissue varies in its response to a particular stimulus. For example, we know that follicle-ripening is produced by the follicle-stimulating principle of the anterior lobe of the pituitary gland. Yet of the many follicles produced only one responds to the full charge of the pituitary hormone and so reaches maturity. The others become atretic. Now the result of Saiki's experiment only proves that an atrophic endometrium which results from castration is insensitive to the stimulus of the bleeding factor of the anterior lobe of the pituitary gland; in other words, that a normal, active endometrium is one of the conditions under which the bleeding factor operates.

It is alleged[7] that if Hartmann's theory were true, the bleeding which follows the administration of anterior pituitary extract to the non-castrated monkey from which the pituitary gland has been removed should be immediate. Instead, it is delayed for some considerable time. Therefore it would seem that the bleeding is due to something subtracted from, rather than something

added to, the circulation. The inference is partly true and partly false. Delayed bleeding only proves that the withdrawal of oestrin, which is produced by the oestrogenic hormone contained in the anterior pituitary extract, conditions the activity of the bleeding factor which the pituitary extract also contains.

The protagonists of the exclusively negative theory of menstrual bleeding say that the bleeding which is produced by extracts of the anterior lobe is microscopic, not macroscopic. Therefore genuine menstrual bleeding must depend upon a different mechanism. Such an argument reminds me of the unfortunate lady in one of Captain Marriot's novels who tried to defend the birth of her illegitimate child on the ground that it was so small. In point of fact, Novak, who is one of Hartmann's associates, tells us that the bleeding, alhough generally microscopic, is sometimes macroscopic and very profuse. Hartmann's theory of an extra-ovarian bleeding factor will help to throw considerable light on the nature of the continuous bleeding which is so characteristic of certain types of functional uterine bleeding.

While I agree with Hartmann that a bleeding factor in the hypophysis is the cause of menstruation, I also contend that the withdrawal of the ovarian hormone or hormones, if not the cause, is an essential condition of menstrual bleeding. The discontinuance of oestrin after a certain amount has been administered to the castrated monkey is always followed by uterine bleeding. The regression, or excision, of the corpus luteum, as well as the excision of the growing Graafian follicle, invariably provokes bleeding. During non-ovular menstruation, as well as intermenstrual bleeding, blood-hormone studies in addition to observations[8] of the sexual cutaneous changes in certain species of the sub-human primates indicate a definite drop in the level of folliculin. These facts can be interpreted only to mean that the periodic waves of depression, in the folliculin-content of the blood, condition the activity of the bleeding factor of the anterior pituitary body. The prevention[9] by oestrin or folliculin of the bleeding which follows the administration of the anterior pituitary extract to the non-castrated monkey from which the pituitary gland has been removed establishes beyond doubt the truth of the theory that folliculin, at any rate, inhibits the activity of the bleeding factor of the anterior lobe of the pituitary gland.

Does the special hormone of the corpus luteum inhibit menstrual bleeding? The bleeding which follows excision of the corpus luteum is not conclusive, since that body contains folliculin as well as its more characteristic hormone, progestin. It is

necessary, of course, to postulate the withdrawal of the luteal hormone as the factor responsible for the endometrial degeneration, accompanied by slight bleeding, which occurs at the end of the luteal phase of the biphasic cycle of the bitch. The hypothesis that progestin inhibits menstrual bleeding in man and the monkey has been tested experimentally by Smith and Engle.

"These observers," says R. W. Johnstone,[10] "administered to mature monkeys anterior pituitary hormones in doses calculated to increase the formation of oestrin, adding large doses of oestrin in the last few days of the experiment. They then discontinued the injections and removed both ovaries. In this way they were able to eliminate a further source of oestrin, while at the same time they provided the appropriate stimulus to uterine bleeding on any theory of withdrawal of oestrin. None the less, they succeeded in preventing bleeding by the injection of large doses of corpus luteal extract which contained only a negligible quantity of theelin." The result of this experiment seems to contradict Novak's view[11] that of the ovarian hormones, oestrin or folliculin is the only one which inhibits menstrual bleeding. As we shall see later, there is a certain amount of clinical evidence that the luteinizing hormone of the anterior lobe of the pituitary gland also inhibits menstrual bleeding.

Relation Between Oestrus and the Menstrual Cycle.

Some few years ago R. W. Johnstone[12] contributed a paper to the *American Journal of Obstetrics and Gynecology*, in which he stated that the human menstrual cycle is monophasic, not biphasic as it is in the lower animals: that the sexual or follicular phase has been missed out in the process of evolution and the reproductive or luteal phase alone survives. In a paper which I contributed to the *British Medical Journal*[13] I advanced many arguments in favour of the view, now generally accepted, that in man and the monkey there are, in reality, two cycles. On account, however, of the partial eclipse of the sexual or follicular phase by the supervention of the reproductive or luteal phase, during the second half of the menstrual cycle the former can only be observed "as in a glass darkly." In monkeys during the non-breeding season, on account of the absence of the luteal phase, the follicular phase can be deciphered quite clearly.

It is generally agreed that uterine bleedings associated with ovarian malfunction are due to a disturbance of the mechanism which maintains the rhythmic phases of the human menstrual

cycle and their nice adjustment to each other. Therefore, in order to understand the aetiology of such bleedings we shall have to analyse, so far as we can, the nature of this complex mechanism.

At puberty the female genital organs, which have been under the influence of the growth-hormone of the anterior lobe of the pituitary body, become sensitive to the stimulus of the ovarian and pituitary hormones. It is now well known that the ovarian hormones depend for their characteristic function upon the pituitary sex hormones. Although the latter have not been successfully isolated for either experimental or therapeutic purposes, the mechanism responsible for maintaining the follicular and luteal phases of the menstrual cycle can only be understood on the assumption of two separate hormones. From the results of Kraul's[14] experiments it would seem that the ovarian hormones, which have been produced in the first instance by the pituitary hormones, in turn react upon the latter so as to heighten their effect. This reciprocal causality explains, on the one hand, the gradual development of the follicular phase during the first half of the menstrual cycle, and on the other, the gradual development of the luteal phase during the second half of the cycle.

How do we account for the fact that prolan B (the luteinizing hormone) becomes active only during the second half of the menstrual cycle? When prolan, which presumably contains both prolan A and prolan B, is administered to immature mice, we notice that many corpora lutea are formed without the intermediate act of ovulation (*corpora atretica* as they are called). There must be some mechanism, therefore, to account for the orderly sequence which occurs in the human menstrual cycle. In a previous communication[15] I referred at some length to the results of Parkes's[16] experiments upon rabbits, which seemed to show that the act of ovulation itself provides the stimulus (probably nervous in origin) which sets free the luteinizing hormone of the pituitary gland.

On account of the supervention of the luteal, upon the follicular phase, the latter is closed to direct observation during the second half of the menstrual cycle.

We know that a definite drop in the level of folliculin occurs at the beginning of the second half of the menstrual cycle. According to Zuckermann[17] this level is maintained throughout the second half of the menstrual cycle. Accordingly the follicular cycle, like that in the lower animals, reaches its maximum development at the mid-point of the cycle. Ovulation, there-

fore, like that in the lower animals, occurs at the height of pro-oestrual development. According to Zuckermann there is sufficient follicular hormone left to delay the pro-oestrual degeneration until the beginning of menstruation. This theory of delayed pro-oestrual degeneration does not seem to have any teleological significance, nor do I know of any mechanism to account for the delay. It can hardly be due to the continued secretion of oestrin by the corpus luteum because the appearance of the next menstruation is not hastened in those cycles in which ovulation does not occur.

In another communication[18] I advanced many arguments, mainly biological, in favour of the view that, except for a temporary arrest at the mid-point of the human menstrual cycle, there is a gradual development of the follicular phase, or cycle, from the end of one menstruation to the beginning of the next. The follicular phase, therefore, reaches its maximum development just before menstruation, not at the mid-point of the menstrual cycle. Ovulation, therefore, instead of occurring at the height of pro-oestrual development, takes place 14 days before the cycle is complete. The follicular and luteal cycles are, therefore, telescoped into each other during the second half of the menstrual cycle. The view which I then expressed, and which rested mainly upon biological considerations, has since been borne out by blood-analysis and other lines of investigation. An examination of the blood by Hartmann has proved that in the monkey the level of folliculin reaches its highest point just before menstruation. The intense colour of the sexual skin phenomena at the same period confirms the blood-findings.

What is the factor which completes the menstrual cycle? What, in other words, is the cause of the pro-oestrual and luteal degeneration which occurs at the same time during menstruation? That it is due to the withdrawal of the anterior pituitary sex hormones is an obvious corollary from the physiological and biological principles which I have enunciated. The problem, however, is only pushed a little farther back. What is the cause of the cessation of activity of the sex hormones? Until quite recently the problem was regarded as insoluble. The work of Kraul seemed to prove that oestrin or folliculin heightens the effect of the oestrogenic hormone of the pituitary gland. Hisaw[19] and others have proved that excess of folliculin inhibits the pituitary function with corresponding inhibition of the ovarian function. When, therefore, the follicular hormone rises to the level attained just before menstruation, instead of stimulating

the pituitary function it inhibits it. It "kills the goose that lays the golden eggs." The folliculin content of the blood rapidly diminishes. Pro-oestrual and luteal degeneration follow as a natural consequence. This thermostatic-like mechanism carries with it many important implications and, as we shall see later, helps to throw considerable light on the cause of glandular hyperplasia—the characteristic feature of the endometrial picture in metropathia haemorrhagica.

THE PHYSIOLOGY OF INTER-MENSTRUAL BLEEDING.

As we shall see later, the close relation between intermenstrual bleeding and certain types of uterine bleeding should awaken gynaecological interest in the physiology of this interesting phenomenon. Microscopic intermenstrual bleeding occurs frequently in monkeys during the breeding season. Macroscopically, it occurs occasionally in women. Though it cannot be proved experimentally, we have no reason to doubt that, microscopically, it occurs in women as frequently as in the monkey. Hartmann was at first inclined to think that intermenstrual bleeding is confined to ovulational menstruation. He, therefore, formulated the theory that the ovary, not the uterus, is the source of the bleeding. One of the monkeys, however, bled intermenstrually for seven days. That event threw considerable doubt upon the ovarian origin of the bleeding. The occurrence, though rare, of intermenstrual bleeding in non-ovular menstruation has shattered Hartmann's original conception. What is the cause of the bleeding? Blood-hormone studies in the monkey supported by the sudden disappearance of the sexual skin changes at the mid-menstrual period indicate that a temporary drop in the level of folliculin ushers in the bleeding. There must be some factor, however, to account for the periodic lowering of the folliculin-content of the blood. Is it due to a temporary inhibition of the pituitary function by excess of oestrin? If such were the case, we should expect degenerative changes in the endometrium. Instead we do not find any endometrial change whatever. In any case, the drop in the folliculin-content is much too sudden, and the bleeding much too prompt, to be explained on the basis of a hormonic mechanism.

What is the teleological significance of the lowering of the folliculin-content at the time of ovulation? We know that folliculin stimulates contractions of the Fallopian tube and uterus. Until progestin, the special hormone of the corpus luteum, has had time to produce its quiescent effect upon the

tubal and uterine musculature, unless the folliculin-content of the blood is rapidly diminished, there is just the danger that the fertilized ovum may be swept out of the uterine cavity before nidation takes place. In a previous communication[20] I expressed the view that in order to prevent such a catastrophe there must be, at the time of ovulation, some mechanism (probably nervous in origin) by which the folliculin is rapidly excreted from the blood by the kidneys. This view is supported by the work of Lowe and Lange,[21] who have demonstrated the existence of oestrin in small quantities in the urine during the premenstrual phase, and at no other time.

Relation Between Intermenstrual Bleeding and the Oestrous Cycle in the Lower Animals.

Hartmann, in the attempt to prove the similarity between the human menstrual cycle and the oestrous cycle in the lower animals, draws attention to the bleeding which occurs in the bitch, not only at the time of ovulation or the end of the follicular cycle, but also at the end of the luteal or reproductive cycle. Here there seems to be an exact parallel to the intermenstrual and menstrual bleedings which occur in man and the monkey. According to Hartmann's[22] interpretation, the luteal phase in the higher animals is a post-oestrual development, as it is in the lower animals. Intermenstrual bleeding, therefore, represents a purely pro-oestrual degeneration. It is homologous with the pro-oestrual bleeding which occurs in the bitch. I do not agree with Hartmann's interpretation. In intermenstrual bleeding there is not any endometrial change whatever. In the pro-oestrual bleeding of the bitch there are marked desquamative changes in the endometrium indicating the suspension of activity of the oestrogenic hormone of the pituitary gland. It is this great difference in the endometrial picture which constitutes the strongest biological argument against Hartmann's view and in favour of the view which I have frequently advocated—that in the higher animals ovulational menstruation represents pro-oestrual and luteal degeneration telescoped into each other.

Metropathia Haemorrhagica.

In several previous communications[23] I have elaborated upon the symptomatology and pathology of this interesting condition. I have pointed out that not only is there an absence of the luteal phase of the normal menstrual cycle, but there is also a very characteristic disturbance of the follicular phase. In the light

of the new physiology of menstruation, such naïve conceptions as congestion of the uterus, or endometritis, as an adequate explanation of the bleeding associated with metropathia haemorrhagica have completely disappeared from gynaecological literature like mist before the rising sun.

I have always thought that there is a close similarity between metropathia haemorrhagica and the persistent pro-oestrual development which occurs in the rabbit and ferret in the absence of copulation. In such animals, the act of copulation appears to heighten the effect of prolan A (the ovulation-producing hormone) to the point required for rupture of the follicle. If this interpretation is correct, then we are entitled to infer that in metropathia haemorrhagica absence of the corpus luteum is due to diminished activity of the ovulation-producing hormone of the pituitary gland. The stimulus, therefore, provided by the act of ovulation to release the luteinizing hormone (prolan B) is missing. Consequently, instead of a luteal phase, there is prolonged pro-oestrual development such as we find in the rabbit and the ferret in the absence of copulation. The view which I have expressed as to the aetiology of metropathia haemorrhagica is directly opposed to that of Novak[24] and others. According to the latter this interesting type of functional uterine bleeding is due to superfolliculism which, in turn, is due to increased activity of the follicle and ovulation-producing hormone. The view which I have propounded receives considerable support from the pathological findings of Wilfred Shaw.[25] The follicular cyst, the distinctive feature of the metropathic ovary, unlike the mature follicle of the normal ovary, is unaccompanied by ripening follicles and the sclerotic ovary of metropathia haemorrhagica has all the appearance of being relatively inactive. These pathological findings are compatible with the view that in metropathia haemorrhagica the sensitivity of the ovary to the stimulus of the follicle and ovulation-producing hormone is below the normal threshold. In any case, these findings cannot be reconciled with Novak's view.

What is the cause of the continuous follicular development or glandular hyperplasia? That it is due to continued activity of the oestrus-producing hormone is generally admitted. But why is there continued activity of oestrin or folliculin? Why, in other words, is the follicular cycle not completed as in normal menstruation? According to the late Professor Graves,[26] in the absence of the corpus luteum the endometrium does not undergo the customary pre-menstrual secretory changes. Under the continued influence of oestrin or folliculin (contained in the per-

sisting follicle), no longer inhibited by the corpus luteum, it acquires, instead, an irregular growth called glandular hyperplasia. This theory rests upon the traditional view that the human corpus luteum controls or inhibits follicular growth. In my opinion, clear evidence in support of this view is wanting.

In another communication,[27] I quoted a case of mine in which surgical removal of the corpus luteum, although followed by premature bleeding, did not appear to accelerate the next period. In non-ovular menstruation, which occurs in monkeys during the non-breeding season (and in some women), the persistent absence of the corpus luteum does not appear to disturb the follicular cycle. On the assumption that the luteal phase is a post-oestrual development like that in the lower animals, the traditional view of the controlling influence of the corpus luteum is a convenient hypothesis to explain the sequence of events which take place between one menstrual cycle and another. The theory, which I have advocated in this and other communications, that ovulational menstruation represents follicular and luteal denegeration telescoped into each other rules out the luteal hermone as the responsible factor for completing the follicular phase of the human menstrual cycle.

For these and other reasons I have always taken the view that the factor responsible for completing the follicular phase is something more fundamental than the special hormone of the corpus luteum or even the luteinizing hormone of the anterior lobe of the pituitary gland: that it is due to a reciprocal relation between the ovaries and the anterior lobe of the pituitary gland, the nature of which future research would enable us to ascertain. Thanks to the work of Hisaw, already referred to, we now know that when the folliculin-content of the blood rises to the level attained at the beginning of menstruation, it inhibits the pituitary function which, in turn, arrests the production of a further supply of folliculin. Consequently both the follicular and luteal cycles are completed. In other words, menstruation takes place. If sub- rather than super-folliculism is accepted as the primary cause of metropathia haemorrhagica, then it is natural to expect that in this condition the folliculin content of the blood can never reach the level attained at the beginning of normal menstruation. Consequently, the follicular cycle is never completed. Instead, under the continued activity of folliculin, there is persistent follicular development or glandular hyperplasia.

What is the significance of the periodic bleeding which occurs

in so many cases of metropathia haemorrhagica? I am inclined to Novak's view that it is an exaggeration of intermenstrual bleeding, not of normal menstruation. If the periodic bleeding were a genuine menorrhagia, then we should expect a complete dismantling of the hyperplastic endometrium which would take some considerable time to regenerate. We should expect, in other words, an exaggeration of the pro-oestrual bleeding which occurs in the bitch. Instead, we find stationary glandular hyperplasia throughout the bleeding and non-bleeding stage. It is true that during the process of bleeding there are localized areas of superficial necrosis. These are probably the effects, not the cause, of bleeding. What is the cause of the periodic bleeding? If we accept the view that the bleeding is an exaggeration of intermenstrual bleeding, then we are entitled to infer that a drop in the folliculin-level owing to its excretion by the kidneys conditions the bleeding. I believe that this inference is supported by blood and urinary analysis. Novak agrees that a drop in the folliculin level conditions the bleeding, but he thinks that the drop is due to temporary inhibition of pituitary function by excess of folliculin—that the mechanism of bleeding, in other words, is exactly similar to that of normal menstruation. Now the arguments which I have advanced in favour of the view that the periodic bleeding of metropathia haemorrhagica is an exaggeration of intermenstrual bleeding are equally effective in proving that inhibition of pituitary function cannot be the cause of the depression of folliculin in the blood. According to my interpretation, in cases of metropathia haemorrhagica associated with periodic bleeding, the folliculin-level has a tendency to rise automatically at what corresponds to the mid-menstrual period of normal menstruation, when a rapid excretion of folliculin from the blood provokes bleeding. In other cases this periodic rise does not seem to take place. The bleeding, therefore, loses its rhythmic character. When it occurs, it may last for a month, two months, sometimes longer. The bleeding stage is succeeded by a correspondingly variable period of amenorrhoea.

It is difficult, on the exclusively negative or passive theory of menstrual bleeding, to explain why normal menstruation only lasts for a few days and the acyclic bleeding of metropathia haemorrhagica may continue for months. On the theory which I have advocated it is reasonable to expect that the bleeding will continue until there is a sufficiency of follicular hormone in the blood to inhibit the activity of the bleeding factor of the pituitary body. In normal menstruation the optimum concentration of

folliculin is reached in a few days. In metropathia haemorrhagica associated with acyclic bleeding, the accumulation of folliculin is naturally slow. Therefore, months may elapse before the optimal concentration is reached. Novak[28] regards a special bleeding factor to account for normal menstruation a physiological luxury. To account, however, for the continuous bleeding associated with many cases of metropathia haemorrhagica he regards an extra-ovarian bleeding factor—distinct from the sex hormones—a pathological necessity.

I have already stated that metropathia haemorrhagica is fundamentally due to a disturbance of the mechanism of ovulation. The fault is, in all probability, due to insufficiency of prolan A (the ovulation-producing principle). In certain cases it may be due to loss of sensitivity of the ovary to its normal stimulus. In either case, there is diminished follicular activity, with the development of a Graffian follicle cyst instead of a normal corpus luteum. Whether the ovary or the pituitary gland is the incriminating organ in a particular case should be ascertained by the therapeutic test of administering prolan A. Unfortunately, this hormone has not been sufficiently separated for therapeutic purposes.

Novak[29] thought that if progestin were available, it should be possible to convert the hyperplastic endometrium into a functional pregravid one and thus complete the cycle. Progestin is not available for general use, as it is obtainable from the corpus luteum in such small amounts.. Besides, it is a highly labile substance. Since the pituitary-like hormone which is found in the urine of pregnant women has a strong luteinizing effect upon the ovaries of the rat and the mouse, it was hoped that it might serve as a substitute for progestin in that it would tempt the cystic ovary to produce its own progestin. By means of this hormone Novak has treated many cases of metropathia haemorrhagica with the most gratifying results. "So prompt is the effect in so many instances," says Novak, "that we were soon convinced that it could not be due to an actual biological change in the ovaries, and direct studies of the ovaries have since then been made bearing out this idea." It seems to me that this haemostatic effect is due to inhibition of the activity of the special bleeding factor by the luteinizing hormone of the pituitary gland.

Intermenstrual bleeding, as I have already pointed out, is characteristically microscopic, and when it becomes macroscopic, lasts, as a rule, only for a few days. The contrast between intermenstrual spotting and the periodic bleeding of metropathia

haemorrhagica which is characteristically prolonged is probably due to the inhibitory influence of the luteinizing hormone of the pituitary gland in the one case and its absence in the other. Quite recently I had under my care a patient who bleeds intermenstrually for several days. She had been bleeding for two days prior to her admission to hospital. One cubic centimetre of the luteinizing hormone (Parke Davis's preparation) was administered on her arrival. Another cubic centimetre was administered at night. Next day the blood was almost black. On the evening of that day the bleeding ceased.

In regard to metropathia haemorrhagica I have had an impressive result with the luteinizing hormone in a young girl who had just begun to menstruate. Previous to her admission to hospital she had been bleeding continuously for six weeks. One cubic centimetre of prolan B, administered twice a day, arrested the bleeding on the third day after admission. She did not menstruate then for about two months. She was bleeding for 12 days before her second admission to hospital. The administration of the luteinizing hormone had led to the same dramatic result. Her next period was quite normal, and she has remained normal ever since.

It is in the bleedings of puberty which have a natural tendency to spontaneous cure that organo-therapy is so pre-eminently successful. In the future many of these young women will be spared the inconvenience of repeated curettage, or the risk of sterility by the administration of radium or X-ray therapy. In my opinion, most of the cases of metropathia haemorrhagica occur in women nearing the menopause. In menopausal bleeding which has not any tendency to spontaneous cure, I agree with R. W. Johnstone[40] that the introduction of intra-uterine radium after preliminary curettage is the speediest and most permanent method of cure. It is very surprising that there are still gynaecologists who perform the operation of hysterectomy, as a matter of routine, in such cases.

Before taking leave of the subject of metropathia haemorrhagica, I should like to make a few remarks about that rare but interesting form in which an ovarian tumour, instead of the normal functioning ovary, forms an intermediate link in the chain of causation. Many such cases have been reported in the literature. Glandular hyperplasia, the characteristic feature of metropathia haemorrhagica, is invariably, or almost invariably, present, and the bleeding is, generally, acyclic in character. These cases occur, as a rule, after the menopause. About six

cases have been reported as occurring before puberty. A few cases have occurred during reproductive life.

In a record of 547 ovarian tumours investigated by Green Armytage,[31] 63 occurred in patients past the menopause. Uterine bleeding occurred in four cases in which the tumours were innocent and in 26 cases in which they were malignant. Green-Armytage advances the theory that an ovarian tumour in a woman after the menopause (and presumably in a young girl before puberty) may take on the function of ovarian-tissue, just as after removal of the thyroid gland for cancer metastatic tumours have been known to function like the absent thyroid gland. Two cases of continuous vaginal bleeding associated with a so-called granulosa-cell tumour in a young woman have been reported by Wilfred Shaw.[32] In another communication,[33] I referred to the case of a young woman who consulted me on account of continuous vaginal bleeding, which had been preceded by a long period of amenorrhoea—the characteristic syndrome of metropathia haemorrhagica. The removal of a small cystadenoma on the left side restored the patient to normal menstrual life. Such cases occurring during active reproductive life cannot be explained on Green-Armytage's view. In any case, his theory cannot explain why only 30 of the 63 ovarian tumours which he found after the menopause were associated with the symptoms and pathology of metropathia haemorrhagica. Novak and Long[34] take the view that granulosa-cell tumours which are characteristically associated with uterine bleeding are derived from "rests" of granulosa-cells which have been left over after the primordial follicles have been formed. The granulosa cell, according to these observers, is a typically feminine cell producing the so-called female sex hormone, folliculin. The hormonal effects produced by tumours of this variety are along the lines of femininity with over-accentuation of certain female sexual characters and functions. The only evidence that the so-called granulosa-cell tumours are derived from granulosa-cell "rests" is the close resemblance which the cells of the tumour bear to granulosa cells. On the theory of Novak and Long, we are driven to the assumption that certain cystadenomata, sarcomata, dedifferentiated ovarian tumours, and even teratomata, reported[35] in the literature as related to metropathia haemorrhagica, the cells of which do not have any resemblance whatever to granulosa cells, are also derivates of the granulosa-cell "rests"—a rather big assumption. It seems to me that further histological and experimental research is needed before we can give a confident

reply to the many questions which these rare forms of metropathia haemorrhagica suggest.

Epimenorrhoea.

There is another type of functional uterine bleeding associated with ovarian malfunction in which there is a shortening of the menstrual rhythm. In many of these patients there is prolonged and profuse bleeding (epi-menorrhagia). Wilfred Shaw has proved by careful histological investigation that in these cases there is premature rupture of the Graaffian follicle as well as premature bleeding. The polycystic ovary, which is invariably present in such cases, as well as premature ovulation, is an indication that this type of functional uterine bleeding is due to superfolliculism, which, in turn, is due to increased activity of the follicle and ovulation-producing hormone of the anterior pituitary body. What is the explanation of the premature bleeding? According to Beckwith Whitehouse,[36] it is due to the presence of ova of low vitality. This view rests upon the assumption, now no longer accepted, that the ovum regulates the periodicity of the menstrual cycle. -In cases of epimenorrhoea or epimennorrhagia, the follicular phase reaches its maximum development sooner than normal. If we accept the view that excess of folliculin inhibits pituitary function, then the sooner the follicular phase reaches the high-water mark of its development the sooner is the cycle completed. Therefore, premature bleeding follows as a logical consequence of premature ovulation.

A number of French workers have succeeded in inhibiting pituitary function in such animals as the rat by the administration of insulin. Influenced by their results, I have administered insulin to a number of cases of epimenorrhoea. The results, which I hope to publish soon, are most encouraging.

Menorrhagia Simplex

The majority of cases of functional uterine bleeding associated with ovarian malfunction can be diagnosed, as a rule, by taking a careful history. Cases of metropathia haemorrhagica associated with periodic bleeding may, however, be mistaken for these obscure functional bleedings in which there is not any histological abnormality, either of the ovary or the uterine mucosa. The periodic bleeding of metropathia haemorrhagica is characteristically prolonged. The periodic bleeding in cases of uterine insufficiency, as they are called, is profuse. Patients often express the

amount of blood lost as if "running away from a tap." The periodic bleeding in metropathia haemorrhagica may, however, at times be profuse. A certain diagnosis, therefore, can only be made by microscopic examination of the endometrial scrapings.

In this connexion I should like to call attention to a condition of the endometrium called stromal hyperplasia, which is occasionally associated with metropathia haemorrhagica. There is a considerable increase in the stroma without any glandular change whatever. Novak is the only observer who has investigated this interesting condition. He has found it present in 4 per cent. of all cases of metropathia haemorrhagica. When such a condition is present, curettage may reveal an endometrium of normal thickness. The scrapings, in consequence, are usually thrown away as of no significance. In 1931 I exhibited,[37] at the Royal Academy of Medicine, a specimen of uterus and ovary from a case of irregular uterine bleeding. The ovary showed the typical follicle cyst of metropathia haemorrhagica. The uterus contained a polypus which showed typical glandular hyperplasia. The rest of the uterine mucosa showed stromal hyperplasia without any glandular changes.

The Cause of Menorrhagia Simplex.

In another communication,[38] I have discussed the aetiology of menorrhagia simplex or uterine insufficiency. Suffice it to say, that serological investigation shows that the majority of such cases are due either to deranged calcium metabolism or to definite haemorrhagic conditions such as purpura haemorrhagica. In this connexion, I should like to stress the fact that several cases of recurrent menorrhagia with severe anaemia have been reported in which there was not any overt evidence of purpura or spontaneous bruising present. Latent purpura, however, was demonstrated by the capillary resistance test. I should also like to point out that splenectomy is the only cure for menorrhagia associated with either typical or atypical purpura haemorrhagica.

Conclusion

A knowledge of the physiology of menstruation and its clinical application has widened the gynaecologist's vision far beyond the pelvic brim. As Novak has said, the gynaecologist of to-day is no longer regarded as merely an operating surgeon. With his wider vision, he no longer wastes time on such sterile discussions as the best means of suspending a displaced uterus. He is much more interested in the nature and cause of these bleedings which the suspension of the uterus has so frequently failed to cure.

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Heartburn in Pregnancy.

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INTRODUCTION.

MANY women suffer from varying degrees of indigestion during pregnancy: one of the symptoms of this condition which has received little attention, although it affects a great number of women, is heartburn.

Heartburn is one of the most persistent and disturbing forms of indigestion from which pregnant women suffer. Indeed, in many cases, this condition causes greater distress than a disturbance of a more serious nature. It is described graphically by many sufferers as a "burning sensation in the chest" which is exaggerated upon lying down.

Those observers who have investigated the gastric juice during pregnancy are all agreed that the acid reaction, both as free hydrochloric acid and combined acid, is reduced during the 40 weeks of pregnancy.

This fact was suggested by Kehrer[1] in 1905, in the days before the Rehfuss tube and the fractional test-meal had been introduced. There has been some difference in opinion as to when the deficiency is most pronounced; Arzt[2] in 1930, and Nakai[3] in 1925, working independently, declared the change to be more marked early, while Castle and Strauss[4] found the maximal decrease in acid during the second trimester, with a rise during the last month before delivery.

Arzt points out that the deficiency in the secretion of acid is most marked at the time when nausea and vomiting are most common, i.e. during the early months, and suggests that dilute hydrochloric acid by the mouth is indicated to prevent the early nausea and vomiting in certain cases.

The Material and Scope of this Investigation.

An investigation into the clinical aspect of heartburn in 100 cases (H.E.R.) has been made in the Antenatal Department of the Royal Free Hospital under the Directorship of Professor Dame Louise McIlroy; this investigation has been correlated by an analysis of the gastric secretion in 40 of these cases (U.S.)

The clinical investigation was by means of a *questionnaire* submitted to 100 pregnant women attending the antenatal clinic and later delivered in the hospital.

The analysis of the gastric secretion was made by fractional test-meals given during the first and third three months, and again two months after delivery. No patient suffered any inconvenience from the tests, other than those of swallowing the tube and sparing the time for the investigations.

Of 100 women who were questioned, 34 did not suffer from heartburn or any other digestive disturbance during pregnancy; the remaining 66 had varying degrees of discomfort due to heartburn alone, or associated with other symptoms of indigestion.

Sixty-six patients complained of heartburn: of these

29.7 per cent suffered only from heartburn.

23.6 per cent suffered from heartburn, flatulence and a feeling of discomfort after meals;

46.7 per cent suffered from heartburn associated with nausea, flatulence and vomiting.

The time of day when heartburn occurred:

(*a*) *Evening*, 67 per cent.

Of these in 63.4 per cent of the cases heartburn occurred after food.
in 36.0 per cent of the cases heartburn was not associated with food.
in 0.6 per cent of the cases heartburn occurred before food.

(*b*) *No definite time of day*, 33 per cent.

Of these in 60 per cent of the cases heartburn occurred after food.
in 8.9 per cent of the cases heartburn occurred before food.
in 8.0 per cent of the cases heartburn occurred before and after food.

The time of day when heartburn was at a maximum:

Morning	18.1 per cent
Afternoon	13.5 per cent
Evening	60.6 per cent
No definite time	7.8 per cent

The influence of diet on heartburn.

Fried dishes and fats brought on, or increased, the condition in 33.0 per cent of the cases.

Food of the most varied kinds, e.g. meat, eggs, cheese, tomatoes and tinned food brought on, or increased, the condition in 40 per cent of the cases.

In 27.0 per cent of the cases food did not affect the heartburn.

Of the 40 patients whose gastric secretion was investigated 27 complained of heartburn at some period during pregnancy or throughout pregnancy. The gastric secretion was examined during the first three months and the third three months and two months after delivery in all these cases.

Results.

1. A. *During pregnancy.*

(*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 10 cases, 37 per cent.

(*b*) Those with moderate HCl or less than 40 c.c. N/10 NaOH, 14 cases, 51.8 per cent.

(*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, 3 cases, 11.0 per cent.

B. *After delivery.*

(*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 1 case, 3.7 per cent.

(*b*) Those with moderate HCl or less than 40 c.c. N/10 NaOH, 7 cases, 25.9 per cent.

(*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, 19 cases, 70.4 per cent.

It is to be noted in this series that whereas only 29.6 per cent of the patients secreted less than 40 c.c. N/10 HCl as a response to a test-meal, two months after delivery, when the secretion can presumably be regarded as the normal for the individual, 88.8 per cent produce this moderate amount of free acid during the course of gestation.

Hyperchlorhydria was at one time commonly regarded as the basic cause of heartburn, but here we have a group of women, all suffering from heartburn and living more or less comparable lives, among whom only 11 per cent can produce a high volume of free hydrochloric acid during the period of symptoms, while after this disability has stopped, the number of cases of hyperchlorhydria rises to 70 per cent.

Thirteen patients in this series did not complain of heartburn throughout pregnancy, and it is interesting to compare their secretion of acid with that of those who suffered from this disability.

2. A. *During pregnancy.*

(*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 6 cases, 46 per cent.

(*b*) Those with moderate HCl or less than 40 c.c. N/10 NaOH, 7 cases, 54 per cent.

(*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, no cases.

B. *After delivery.*

(*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 3 cases, 23 per cent.

(*b*) Those with moderate HCl or less than 40 c.c. N/10 NaOH, 3 cases, 23 per cent.

(*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, 7 cases, 54 per cent.

Here the incidence of lowered acid secretion is much higher. although it must be taken into account that the normal secretion in the cases, indicated by B, showed a lower percentage of high acidity, and two cases (15.4 per cent) were achlorhydric.

Whereas in this group 54 per cent of the patients, who could normally secrete a good volume of free hydrochloric acid, failed to maintain this high secretion during pregnancy, in the group of cases of heartburn 11 per cent maintained a high secretion through the period of gestation. In this group there were two patients who were true achlorhydrics, who, in addition to not suffering from heartburn, did not suffer from any other gastric abnormality. Both these patients showed an early anaemia which responded well to treatment with iron, this deficiency being related to impaired absorption of iron from the food, on account of the decreased gastric efficiency. It would not have been unexpected if these two women had suffered from heartburn and indigestion, but it can only be recorded that they both had uneventful gastric histories throughout the period during which they were watched.

Following the clinical investigation we find one or two further points which may be of interest to the clinician.

As a result of the *questionnaire,* it was found that there was considerable variation in the period of gestation when the heartburn first occurred, as will be seen from the following figures:

First occurrence of heartburn.

At the	third	month	...	...	39.6 per cent
,,	fourth	,,	...	...	8.3 ,,
,,	fifth	,,	...	...	37.5 ,,
,,	sixth	,,	...	...	6.25 ,,
,,	seventh	,,	...	...	6.25 ,,
,,	eighth	,,	...	...	0.0 ,,
,,	ninth	,,	...	...	1.0 ,,

Period of gestation when heartburn was at a maximum.

Early (period not stated)	...	...	15.1 per cent
Fifth month	...	...	20.2 ,,
Sixth to eighth month	...	...	45.5 ,,
Ninth month	...	...	19.2 ,,
After ninth month	...	...	0.0 ,,

Examining the results from the analysis of the gastric secretion separately for each trimester, we find the following:

1. *Those who suffered from heartburn, 27. During the first three months.*
   (*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 18.2 per cent.
   (*b*) Those with moderate HCl or less than 40 c.c. N/10 NaOH, 55.9 per cent.
   (*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, 25.9 per cent.

   During the third three months:
   (*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 51.8 per cent.
   (*b*) Those with moderate HCl or more than 40 c.c. N/10 NaOH, 44.4 per cent.
   (*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, 3.8 per cent.

2. *Those who did not suffer from heartburn*, 13.
   During the first three months:
   (*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 38.5 per cent.
   (*b*) Those with moderate HCl or less than 40 c.c. N/10 NaOH, 38.5 per cent.
   (*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, 23 per cent.

   During the third three months.
   (*a*) Those with low HCl or less than 20 c.c. N/10 NaOH, 53.8 per cent.
   (*b*) Those with moderate HCl or less than 40 c.c. N/10 NaOH, 46.2 per cent.
   (*c*) Those with high HCl or more than 40 c.c. N/10 NaOH, no cases.

The connexion between gastric acidity and the occurrence of heartburn.

It is seen from the above tables that the variation in the acid value of the gastric juice during pregnancy is not necessarily associated with the occurrence of heartburn.

Of 39 per cent of women who first complained of heartburn during the third month 74.1 per cent secreted less than 40 cubic centimetres of N/10 HCl as a response to a test meal, whereas 64.7 per cent of women had a maximal degree of heartburn between 28 and 36 weeks when 96.2 per cent secreted less than 40 cubic centimetres of N/10 HCl.

Among those women who did not suffer from heartburn 77 per cent secreted less than 40 cubic centimetres N/10 HCl, and during the third three months this figure changed to 100 per cent showing a low acid juice.

It was noted that, in the majority of cases, heartburn caused less disturbance after the 36th week of gestation.

Period when heartburn ceased.

Two or three weeks before delivery ...	75 per cent
No improvement	25 per cent

In all of the cases of heartburn in which treatment was given, an alkaline preparation was used. Relief was obtained with the following preparations:

1. ℞ Sodii Bicarbonatis ... ... gr. xv Spiritus Chloroformi ... ... ♏. v Infusum Gentianae Compositum ad ℥i *Sig.* ℥i t.d.s.	In 10.6 per cent of the cases
2. ℞ Bismuthi Carbonatis ... ... gr. xv Magnesii Carbonatis Levis ... gr. x Sodii Bicarbonatis ... ... gr. x Aquam Chloroformi ... ... ad ℥fs *Sig.* ℥fs t.d.s.	
3. ℞ Sodii Bicarbonatis ... ... gr. xx Potassii Citratis ... ... gr. xl Calcii Sodii Lactatis ... ... gr. viifs Lactosum ... ... ad gr. lxxx *Sig.* ℥i t.d.s. *ex aqua* in ℥iv.	In 31.8 per cent of the cases

Relief was not obtained with medicine in 29.4 per cent of the cases. Medicine was not taken in 28.2 per cent of the cases.

The administration of dilute hydrochloric acid (30 minims in a glassful of water during meals) has been carried out on another group of patients suffering from heartburn during pregnancy. These cases, however, are not recorded in this series.

Toxaemic patients.

Seven and a half per cent of patients complaining of heartburn developed toxaemia during the later months of pregnancy.

Conclusions.

Heartburn is a condition affecting a great number of women during pregnancy: of 100 women who replied to a *questionnaire* 66 stated stated that they suffered from this disturbance at various periods when they were pregnant.

Heartburn was first complained of by 39.6 per cent of the patients during the third month, by 37.5 per cent during the fifth month, by 21.9 per cent during the sixth and seventh months; after this period its first occurrence was noted in only one case, although when it occurred during the earlier months it often continued until the pregnancy was well advanced.

The severity of the heartburn was at a maximum from the sixth to the eighth month in 45 per cent of the patients. In the remaining cases, 35.3 per cent found the disturbance most marked up to the 20th week and 19.2 per cent at the 36th week.

There was complete relief from heartburn two or three weeks before delivery in 75 per cent of the cases; this was, in most cases, independent of any treatment.

In the greater number of cases, it was difficult to find any dietetic factor influencing this condition, but in 33 per cent of the patients fried foods and fats brought on the heartburn or made it worse.

The heartburn was relieved by a compound mixture of alkalies and calcium in 31.8 per cent of the cases and by a mixture containing bismuth or alkaline gentian in 10.6 per cent of the cases. In 29.4 per cent medicines did not give relief; the remainder were untreated.

Seven and a half per cent of patients complaining of heartburn developed toxaemia during the late months of pregnancy.

Gastric analysis. If the figures obtained from analysis of the gastric juice two months after delivery may be regarded as the

normal for the individual, it is seen that the secretion of acid is definitely decreased during pregnancy, the decrease being more marked in the third than in the first trimester. It is of importance to note that this lessening of acid secretion occurs in those patients suffering from heartburn and those who do not; from this we may conclude that the diminution of acid secretion is not necessarily associated with heartburn.

We are indebted to Professor Dame Louise McIlroy for her permission to undertake these investigations.

The gastric analysis was part of an investigation carried out by Miss Shelley while holding the Mabel Webb and A. M. Bird Research Scholarship.

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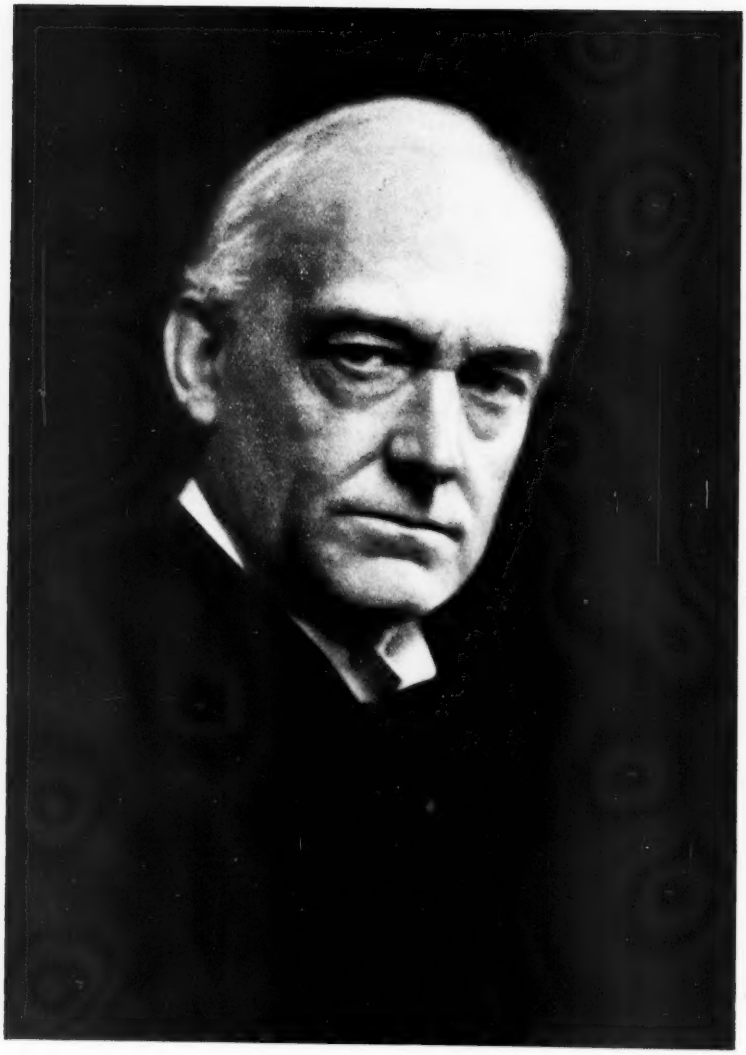

THE RIGHT HONOURABLE LORD RIDDELL

Obituary

Baron Riddell, of Walton Heath.

GEORGE ALLARDICE RIDDELL was born at Duns in Scotland on May 25th, 1865. The son of a Civil Servant, he was the architect of his own fortune. Educated in London, and having decided to become a solicitor, he entered the firm of the late Mr. Wooler, of John Street, as a solicitor's clerk, and was given his articles by that gentleman. During his apprenticeship he read for his examination, on which, having passed, he became a solicitor at the earliest legal age, when he was 21 years old. He at once entered into active practice, and being endowed with gifts which raised him above most of his contemporaries, he built up a large practice, and eventually became the senior partner in the firm of Riddell, Vaizey and Smith. During his practice as a solicitor he acted as the legal representative in London of the Corporations of Huddersfield and Cardiff, and of the *Western Mail* of this city, and it was this latter connexion which turned his thoughts towards journalism, which remained for the rest of his life his principal interest, and of which he was one of its greatest representatives.

His introduction to journalism began under the most auspicious circumstances, in that he had formed a great friendship with Mr. Lascelles Carr, the managing director and part proprietor of the *Western Mail*, probably the ablest journalist of his day, and in 1890 Riddell began his association with that journal. In 1896, a fire having destroyed the premises of the *Western Mail*, a new company was formed, and Riddell became one of its directors, succeeding to the chairmanship on the death of Mr. Carr, and for the next 16 years he acted as its managing director, devoting himself to the development and interests of this paper. During this period Riddell, in association with Mr. Lascelles Carr and Sir Emsley Carr, purchased the *News of the World*. The greater portion of his journalistic career was devoted to the interests of this paper, and how successful these were is instanced by the fact that it has the largest circulation of any paper in the world, the weekly circulation rising from 30,000 to 3,500,000, and those who have travelled abroad will know how this paper can be

obtained practically in any part of the civilized world when any other English paper is not available. Although in time, owing to Riddell's great knowledge of the law and his intimate knowledge of municipal affairs, the firm of Riddell, Vaizey and Smith became the leading firm of solicitors in London, the fascination for journalism became so great that, eventually, Riddell retired from active practice, though not from the study of the law, and thereafter journalism became his chief occupation, in which he gained an oustanding reputation for acumen and sound judgment. Indeed it was these attributes which resulted in his being appointed a member of the Admiralty, War Office and Press Committees during the War and as the British Press Officer at the Peace Conference. Although in appearance Riddell was an apparently delicate man, he had an inexhaustible source of energy and added to his other Press activities the Chairmanship of the Newspaper Proprietors' Association, of the Periodical Trade Press and of the Weekly Newspaper Proprietors' Association, and a Directorship of George Newnes, Ltd., of C. Arthur Pearson, Ltd., and *Country Life*, Ltd. The outstanding success of Sunday newspapers is almost entirely due to the method he devised of distribution through direct agents.

Knighted in 1909, Sir George Riddell rendered an invaluable service to the Press, and through it to the nation, both during and after the War. As liaison officer between the Cabinet and the Press the duties connected with this office were always delicate and at times so difficult as to be almost insurmountable, but his great tact and good temper overcame them all, and in appreciation of the distinguished services thus rendered he was entertained by the Press of the country and presented with his portrait, painted by Sir William Orpen. Sir George Riddell was created a baronet in 1918 and a peer in 1920, when he was granted a coat of arms bearing an ancient printing press, with two printers at the time of Caxton as supporters, and as a crest a carrier pigeon carrying an open scroll in its beak.

In 1921 Lord Riddell served as liaison officer at the Washington Conference on Naval Disarmament, between the Conference and the Press of all nations, and as a gesture of their gratitude the representatives of the Press presented him with a handsome gift at the close of the Conference. One of the most remarkable tributes ever paid Lord Riddell was by the Newspaper Proprietors' Association, of which he was Chairman, when the proprietors and editors of all the leading newspapers, with Major Astor of *The Times* in the chair, entertained him to dinner and

presented him with one of his most cherished possessions, a silver salver, on which were engraved the signatures of all these leading men.

As has been stated, although Lord Riddell forsook the practice of the law for journalism, the study of the law remained one of his interests. His book *Law for the Million* has attained a very large circulation, and he was particularly interested in medico-legal questions, being a member of the Medico-Legal Society, one of its Presidents, and among the most constant attendants at its meetings.

Second only to his activities in journalism was his unfailing interest in those who could not help themselves, and his fearless advocacy on behalf of his less fortunately placed fellows won for him a host of admirers in all sections of society. It was this interest which resulted in his being appointed President and Chairman of the Royal Free Hospital, the most fortunate incident in the history of this institution. For many years he devoted a large amount of his time and a vast amount of energy to this hospital, and was the means, both by his personal munificence and donations from his friends, of contributing some half a million pounds sterling to its funds. In addition to a donation of £3,785 to found a Children's Ward, £14,000 to complete the fund to endow the Grays Inn Road Clinic, together with Sir Albert Levy, he gave, in equal shares, £100,000 to endow the Eastman Dental Clinic, a unit of the Royal Free Hospital which had been erected by Mr. Eastman at a cost of £250,000. His connexion with the Royal Free Hospital led to an increased interest, as a layman, in medical affairs and politics, in virtue of which he was made an Honorary Fellow of the British Medical Association, and Chairman of the Liaison Committee in the delicate negotiations between the Voluntary Hospitals of London and those of the London County Council.

No mention of the activities of Lord Riddell would be complete, however, to a large number of the readers of this Journal without reference to his sympathetic connexion with The British College of Obstetricians and Gynaecologists. He was its greatest benefactor and its first Honorary Fellow, of which distinction he was always very proud. As Treasurer of the College, on its foundation, I had on many occasions to discuss with him its prospects and was the recipient of much sound advice, which was of inestimable value also to others of its founders. His sympathy with their ideals was not only directed to the fact that he was

imbued with the firm belief that the time was over-ripe for the science and art of obstetrics and gynaecology to take that position in the medical oligarchy to which it was entitled but, perhaps more particularly one gathered, from his intense desire to take his share in any movement which had, among its objects, the lowering of the maternal mortality and morbidity and the provision of healthy and useful citizens for the nation. Combined with his munificence he was possessed of a very practical mind and he was always ready to contribute to any scheme which would redound to the credit of the State. Thus when he promised me £10,000—later raised to £14,500—for the College he remarked, "I will give you sufficient money to run the College for seven years, after which, if it has not made good, it is not deserving of further support." Up to his last illness I had many opportunities of meeting him, and it was a matter of the greatest satisfaction to him to know that the College had "made good." He always showed his unfailing interest in the College and discussed various ways in which it might extend its utility and enhance its position. One was always met with the remark, "How's the College?"

In spite of so many interests and activities, Lord Riddell found time for literary work. He published essays from time to time, which were collected under the titles of "Some Things that Matter" and "More Things that Matter," in which he dealt with a large range of subjects. He wrote a monograph on Medico-Legal subjects, contributed to this Journal, and whiled away some of his hours of sickness by writing a novel entitled "The Curious Story of Helen Tulk." But his most important contribution in this direction were his diaries. In June 1933 he published "Lord Riddell's War Diary: 1914 to 1918." In November of that year "Lord Riddell's Intimate Diary of the Peace Conference and After: 1918 to 1923"; and in November 1934 "More Pages from My Diary," the profits from which, of all three, he characteristically devoted to the Newspaper Press Fund, thus showing his interest up to the last in those who had worked for him personally and for the Press generally. Possessing an unequalled and intimate knowledge of events and men during those fateful years and being a shrewd and impartial observer, because of their human interest and unbiassed judgment, many competent authorities maintain that these Diaries are among the most important contributions to this period of our history and will be of lasting service to it.

Lord Riddell's chief recreations were hard work and golf.

CORRIGENDA.

Baron Riddell of Walton Heath.

The publishers regret that owing to an oversight on the part of a proof reader, the following mistakes appeared in the February issue of this journal:

Page 118, line 11, should read "Thus when he promised me £10,000—the grant of £600 a year being raised later to £1,400—for the College he remarked, "I will give you sufficient money to run the College for seven years, after which, if it has not made good, it is not deserving of further support." The total donation was, therefore, £10,800 instead of the original £10,000.

He was the chief proprietor of the Walton Heath Golf Club, President of the London Golfing Society, with Sir Emsley Carr founded the Artisan's Golfing Society, and was the means of establishing the public course at Richmond. His interest in golf professionals was shown when he founded the *News of the World* Tournament. Interested in gardening, he took many prizes at the Royal Horticultural Society's exhibitions and elsewhere.

Lord Riddell was an Officer of the French Legion of Honour and held the Grand Cordon of the Crown of Italy. He leaves no heir to the peerage and is survived by Lady Riddell, a daughter of Mr. D. W. Allardice of Rock Ferry, Cheshire.

And so passed away on December 5th, 1934, a remarkable personality, a man of great public spirit, possessed of a mind which was both logical and practical, with a character the keynote of which was thoroughness, nothing being too large or too small to receive his attention, a great thinker, an omnivorous reader with an intimate knowledge of many subjects, one who was welcomed by the leading men in politics, medicine and commerce for his sound judgment and sympathetic advice, who was beloved by all who knew him and worked for him, a master of conciliation, of untiring energy and great courage, one who had an interest in every one of the wide circle in which he moved, and of unusual loyalty to his friends, of great charm, a kindly personality with an intense sense of humour, a perfect host, a munificent benefactor and a great gentleman. *Requiescat in pace!*

Comyns Berkeley.

Lord Riddell's many and varied interests have justly been stressed, and outstanding among them was an intense interest in his fellowmen, individually and collectively. None reading his published extracts from his diaries can fail to be struck by his obvious interest in every one of the wide circle in which he moved. His remarkable success in journalism may in part be ascribed to his keen understanding and appreciation of his fellow-citizens in the mass and how they thought. His interest in Medicine, too, appeared to me to arise out of this wider one, for it was largely its sociological and medico-legal aspects that appealed to him.

To us of the medical profession his accurate perception of

trends of thought, his acquaintance with methods of practice, and his ability to quote chapter and verse for his sources of information were always remarkable. Nowhere were these faculties better shown than in one of several highly instructive contributions to the Medico-legal Society, that on "The Legal Responsibility of the Surgeon," in which special attention was given to the legality and possible consequences that might arise from 'request' operations for the sterilization of healthy women by too compliant surgeons. A section from a well-known text-book of midwifery was quoted with approval, another discussed critically, and the conclusion reached that under the laws against 'maiming', operations of this kind were illegal, and that the question of their justifiability could "not be left exclusively in the hands of the high-priests of obstetrics and gynaecology and their prompting and consenting patients." The recent Departmental Committee's (Brock) Report on the Voluntary Sterilization of Mental Defectives decided that legislation was necessary for such cases, thus confirming Lord Riddell's view of some years earlier.

His knowledge of what was going on in Medicine was particularly well shown in matters obstetrical and gynaecological, in which he may be said to have 'specialized', for, as he used to say, his weekly study of the *Lancet* and *British Medical Journal* tended to lead him to imagine himself afflicted with the diseases he read about, whereas he suffered no such qualms in his obstetrical studies. His paper on "The Legal and Ethical Aspects of Abortion", read at a joint meeting of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine in 1927, will be remembered by all who heard it, both for its historical and ethnological review of customs and enactments in various races and countries, and its insight into the problems that face obstetricians in view of the widespread decline in ethical standards in this regard. He also gave evidence before the Departmental Committee on Maternal Mortality and Morbidity, in which he urged the importance of an inquiry into the effects of provoked abortion in maintaining the static maternal mortality-rate, both from the greatly increased resort to it and possible latent sepsis that might remain and be lit up in subsequent pregnancies. Some of this evidence was published in his paper that appeared in the *Journal* in 1931 (Vol. 38, pp. 1–6), entitled "Abortion and Maternal Mortality."

By the obstetricians and gynaecologists of this country Lord Riddell was known and honoured as a true friend and helper in

a time of need. They went to him when the British College of Obstetricians and Gynaecologists was as yet in the air. He recognized at once that, scattered as they were through the Royal Colleges in England, Scotland and Ireland, where they had little say, obstetricians could exert the influence that was their due only by a College of their own that could speak for them. He encouraged them by the promise of help and by advice through the difficult times preceding incorporation. His promises were much more than fulfilled, particularly when he thought the time had arrived when the College should have a house of its own. His architect was employed to look at possible houses, and through his encouragement and his generosity, together with assistance from an anonymous donor, the College was housed. That he judged rightly there can be no doubt, for nothing since its foundation has served more to establish it firmly. As its first Honorary Fellow and its first and greatest benefactor, Lord Riddell's name will be prominent in the annals of the College, for it was he who made possible the stage reached to-day. The sadness of parting with so good a friend is hard to bear. He leaves pleasant memories and deep gratitude in the hearts of all in the British College of Obstetricians and Gynaecologists.

The President of the British College of
Obstetricians and Gynaecologists.

It is difficult to put down in black and white all one would like to say of Lord Riddell, whose character was so unique and complex. How one admired his own gift of expression and ready pen. It has been a privilege in life's journey to have met such a dynamic personality and to have been accounted as one of his friends.

How untiring was his energy and his capacity for work. No detail was too small to be of interest to him, and the humblest worker could offer him facts which gave him a fresh viewpoint of life. His aim was to know something of everything, and it was to experts he always went for his information. He had the royal faculty of putting people at their ease at once and of drawing out their ideas and opinions. The only thing he could not abide was humbug.

He had the true journalistic mind for new discoveries which could be passed on to the readers of his various publications. If one mentioned to him an incident or a subject out of the ordinary run of life he would say: "That is a good idea, I will put someone on to that and have it written up." Some new thought would be jotted down on the back of an envelope, perhaps, or on the margin of a magazine. He took infinite care to verify his facts and references before he published any of his own writings.

Lord Riddell was not a party politician although interested in politicians themselves. For this reason he seldom took his place in the House of Lords, as he always said that to achieve success in the Upper House one must belong to a party.

He was intensely Imperialistic in his outlook, and had a great admiration for the solid, steady character of the British nation. Although in no political sense a Socialist, he was always a friend and advisor of the working man, by whom he was much beloved.

When troubles appeared on the horizon of the newspaper and printing worlds, and impending strikes began to be whispered abroad, it was sufficient to place him in the chair at a meeting. Often his quick wit and humour turned temper into laughter and peace was restored. His praise of the achievements of others was unstinted and generous, even towards those who held opinions diametrically opposed to his own. He had an admiration, not so much for genius as for those who had the art of taking pains. Men and women of all classes not infrequently sought his advice in family or business difficulties and, when financial help was not the object of the interview. Many a one lives to bless him for his kindly counsel which was the means of averting domestic estrangements or personal tragedies.

It was just sufficient to give him the facts of the struggle for existence on the part of some poor patient in the Royal Free Hospital to find later that employment had been found or help accorded in a way which never came to the knowledge of the public.

Lord Riddell was a mixture of several personalities. He was an optimist, full of the joy of life and proud of his success and influence. He was almost spartan in his simplicity of living. He spent very little on his own amusements. Golf was his only relaxation. He was a teetotaller, and had no knowledge of games of cards. Of late years he carried a snuff-box, and advocated its use as a means of clearing the brain. He was a perfect host. He valued friendship very highly and was strangely pleased

when given any little manifestation of affection on the part of his friends. He had a magnetic personality.

I still think I see him sitting at the fire on a Sunday afternoon with several people around him who were spellbound at his vivid description of men and their doings. When it was time to go he would jump up and say: "Forward is our watchword," an expression which is the legacy he has left behind him for those who feel the loneliness of his passing.

He faced the facts of life with the dauntless courage he showed when overtaken by physical illness. His gallant fight to carry on his public responsibilities to almost the last has been the admiration of everyone.

Lord Riddell has left behind him a precious and undying memory in the hearts of those who knew him best.

Dame Louise McIlroy, D.B.E.

LORD RIDDELL was an outstanding figure in so many departments of public life, his intellect was so brilliant, his mental ability so exceptional, he was so remarkably alert and so quick to grasp the salient points in any discussion, that his death is truly a national calamity. An extremely generous man, many charities will feel his loss, most of all the Royal Free Hospital, to which for the last 10 years, as President and as Chairman of the Weekly Board (two offices never previously held by the same man) he had given of his best, alike in time, money, influence, and careful attention to all the details of administration. He was particularly interested in the work of the Obstetrical and Gynaecological Unit, the first of its kind to be started in London, for any steps towards the reduction of maternal mortality always had his active sympathy. Hence he was intensely proud of his election as an Honorary Fellow of the College of Obstetricians and Gynaecologists, and used to tell with great gusto the story (whether apocryphal or not I cannot say) of how he had been written to at his residence at Walton Heath and asked to undertake a confinement.

He seemed to have a special liking for doctors and their work, and was a frequent and much appreciated guest at medical functions.

Beneath a mask of cynicism he concealed extreme kindness of heart, especially to the poor, the sick, and the suffering, and

his generosity was by no means confined to the giving of large sums of money to important charities. Nothing seemed to please him more than to secure a few shillings a week extra for a poor pensioner or a decrepit charwoman. Many a humble person had reason to be grateful to him for small acts of kindness which served to brighten and enrich their oft-times rather dreary lives.

The years pass rapidly and inexorably by, but long after Lord Riddell's appearance becomes merely a tradition, his name fortunately will be handed down to posterity by the "Riddell Ward" and the "Langton-Riddell Nurses' Home" in the Royal Free Hospital, the prosperity of which he did so much to promote.

J. Walter Carr, M.D.

LORD RIDDELL was always a good friend to the Nightingale School at which Lady Riddell received her training. He took much interest in its traditions and its more recent developments. He was the generous donor of many valuable letters written by Miss Nightingale, and of rare portraits of the Foundress of the School—treasures indeed which greatly enhance the Nightingale collection already in its possession.

He rarely failed to accompany Lady Riddell to the Nurses' Annual Christmas Entertainment at which he was a much honoured guest, the performances being produced by the Nurses' Dramatic and Musical Societies. His appreciation of the artistry and creative powers displayed by the nurses was shown some years ago by a generous gift that put these societies at once on a sound financial basis and enables them to give yearly substantial aid to other recreative activities of the School. Thus the School possesses in more ways than one a permanent memorial of his warm-hearted interest and great kindliness.

Dame Alicia Lloyd Stead, D.B.E.

IT is a very difficult task to write about one with whom, in certain matters concerning the work of Public Health and Public Authorities, I differed profoundly, and yet with whom I was always on terms of very great personal friendship.

My first real contact with the late Lord Riddell began some time during the year 1925, although I had known him for many years before then in the same sort of superficial way in which we all know hundreds of persons in the course of life's journey. The particular circumstances which brought us so much more closely together, and which ultimately ripened into a deeply affectionate regard for each other, was the discussion which began about that time with reference to the provisional proposals of the then Minister of Health concerning the Reform of the Poor Law.

Lord Riddell was always intensely interested in what I may call for convenience "Public Affairs", whether Local, National, Imperial or International. His long and varied experience of such matters was, as everyone knows, of an exceptional character. His position, first of all as a practising Solicitor, then as a great Journalist, and later as an intimate friend of Cabinet Ministers (of all political parties), gave him unique opportunities of acquiring knowledge and information, coupled with sound judgment and a wise discretion, as well as a remarkable instinct, for divining the trend of public opinion.

Therefore, it is not surprising that he was intensely interested in this great project for the Reform of the Poor Law, a subject which had been discussed all over the country for many years, before and after the Great War, by all the political parties in power at various dates between 1900 and 1925. Lord Riddell very quickly appreciated the importance of the fact that, when these provisional proposals were ultimately translated into an Act of Parliament, one of the outstanding features of the Act would be the establishment in London, for example, of a centralized Municipal Hospital Service, under the direction and control of the London County Council, which would not only be greater in magnitude than anything of the kind ever seen before, but also that such a Hospital Service might be more far-reaching in its ultimate results than most people had any idea of at all.

To this particular development of a Centralized Municipal Hospital Service he took no exception. On the contrary he fully realized and believed that, properly organized and directed, such a Hospital Service could not be otherwise than an immense forward step upon the system then in operation.

On the other hand, he was genuninely apprehensive as to the ultimate effects of such a Centralized Municipal Hospital Service upon the Voluntary Hospitals of London. For various reasons the Local Government Act (1929) which translated these provi-

sional proposals into an Act of Parliament, did not come into operation until the 1st April, 1930, and at about the same time the Voluntary Hospitals Statutory Committee (Clause 13 of the Act) came into existence with Lord Riddell as its first Chairman.

This Committee was intended to form the link, as it were, between the L.C.C. (as representing the Public Hospital Service of London) and the Voluntary Hospitals of London, and such a Committee was clearly designed and introduced into the Act of Parliament with the specific object of promoting co-operation between the Public Hospitals Service and the Voluntary Hospitals for the benefit of the sick poor. Most unfortunately, however, it must be confessed that from its inception it was not a success. I have no intention of expressing any opinion as to why it was not a success, but there is no doubt at all that at first the result was the reverse of co-operation, or indeed harmony, in any sense of the word.

Ultimately, however, wiser counsels prevailed and the relation between the L.C.C. and the Voluntary Hospitals Statutory Committee became sane and satisfactory. It is a real pleasure to recall the fact that at the last meeting between these two bodies, which took place in July 1934, Lord Riddell afterwards expressed to me his great satisfaction that harmonious co-operation in the present and future was now assured.

There was another matter in which, I regret to say, we differed profoundly, and that was the best method of appointing a Consultant and Specialist medical staff to the L.C.C. Hospital Service.

It would be ungracious to enter into any discussion now on these matters. It is sufficient to say that however profoundly anyone differed from Lord Riddell, he could always rely upon one thing, and that was that at all times Lord Riddell was inspired in his views by a passionate desire to help the sick and suffering and those who, for some reason, had fallen by the wayside; to promote the welfare and happiness of his fellow human beings, and especially the 'under-dog'.

If I may be allowed in this appreciation to be personal for a few sentences, I should like to record the fact that I shall always look back to the end of my days with feelings of the deepest gratitude to him for the many interesting and most enjoyable Sunday afternoons which I, in common with many others, spent with him at his home at Walton Health. During those long afternoons together he would discourse upon nearly every subject under the sun—medical, legal, political, and personal. More-

over, his marvellous business ability, extraordinary and extensive knowledge of individuals, wide experience of the problems of daily life, mature judgment, wise discretion, and, above all other characteristics, his immense sense of humour, made him not only a charming, delightful, exhilarating and amusing companion, but also an invaluable friend and adviser.

I know of no man whom I have ever met in my life to whom I would have preferred to go for advice and guidance in time of trouble than the late Lord Riddell. I shall always treasure the affectionate friendship which existed between us as one of the happiest memories of my life, and I am confident that there are many scores of men and women in all walks of life who would say the same of him.

Sir Frederick Kay Menzies, K.B.E.

It is difficult for me to add anything to the admirable biography of my old friend and colleague, Lord Riddell, which Sir Comyns Berkeley has written for this Journal.

Knowing Lord Riddell so well, he has been able to describe his many interests with a thoroughness which other writers have not been able to do, and his close association with him in many walks of life enabled him to study more closely than others the remarkable gifts of this remarkable man.

I was associated with Lord Riddell for over 43 years. He and I were in intimate partnership the whole of that time, and we lived together before my marriage.

If, as a result of this long friendship, I were asked to describe his character in a few words, I should say that he was never content with second place. He adopted in life the motto of the Coldstream Guards, *Nulli Secundus*.

To achieve his end he never spared himself. He turned night into day when he was engaged in building up a great legal practice, and when, after he had recovered from an illness which was the direct result of the absorbing attention he had given to his clients' interests, he entered upon newspaper work, he devoted all his energy to mastering the details of this profession.

Never very robust, he naturally had to live a life of simplicity, if not of ascetism. He neither drank nor smoked, and the pleasures of the table had but little interest for him.

There were few subjects, however, which did not command

his interest, and no subject in which he was interested which he did not adorn.

The wonderful tribute paid to his memory at the journalists' church of St. Bride's was one indication of the affection and admiration he inspired among members of the Press the world over.

Sir Elmsley Carr.

BOOK REVIEWS

"A Textbook of Gynaecological Surgery." By Sir Comyns Berkeley and Victor Bonney. Cassell and Co., Ltd., 3rd edition, 863 pages, 530 new and original drawings by Victor Bonney, and 17 coloured plates. Price £2 2s. 6d.

This is indeed a *magnum opus*. It represents the best work of two men who have been pioneers and creative artists in the field of gynaecological surgery, catholic in their criticism and scientific in their judgment. Followers of a great tradition, Berkeley and Bonney have raised the practice of operative gynaecology to a higher plane than that attained by any other branch of the surgical art. We are not so unimaginative as to suggest that this record marks the end of the journey: the road still winds uphill. The science of gynaecology must proceed; and, even as we write, physiological research is tending to displace the need for surgical measures in various directions. Nor is woman, with all her psychological peculiarities, a machine that may be subjected to invariable technical adjustments. It is idle to suppose that the mortality figures so honestly registered in this very textbook admit of no improvement; and, on the other hand, we shall venture to criticize some matters of opinion therein expressed. Nevertheless, it is difficult to visulalize a field for further advances of any considerable importance in the major operative procedures that have been elaborated and so ably portrayed by the authors.

The greatest surgeons have not uncommonly possessed *inter alia* the qualities of great engineers, and unfortunately in their publications and utterances they have all too frequently given expression to this aspect of their work, without conveying to their students and readers the vital importance of that experience, judgment, and knowledge of human nature in all its manifestations, which must inevitably form the basis of the science and art of surgery. For this reason many of their followers and imitators have been led astray, to the detriment of the public, though possibly not to that of their own pockets. On this score we can absolve our present authors entirely and completely. Every chapter of this book bears evidence of clinical observation, ripe experience, considered judgment, and intellectual honesty; and to these essentials they have given ample expression.

Our congratulations are due to the publishers of this textbook. It is admirably printed and produced, and the illustrations are really excellent. For the latter, Mr. Bonney is chiefly responsible. To his credit there are 530 black-and-white drawings of such outstanding merit as to render almost unnecessary a study of the text! The labour involved must have been colossal. There are two new coloured plates, also by Bonney. The whole of this edition has been practically rewritten. The pages, which are considerably larger, number 863, as against 829 in the last edition. The index

is unusually adequate. The dedication is gracious and inspiring; and we trust that the powerful lines quoted at the end of the book will animate rather than dishearten those who are struggling uphill in the heat of the present day.

It is gratifying to find that consideration is given, at the outset of the book, to the psychological attributes of a good surgeon. These essential qualities are all too frequently taken for granted, or underestimated, in this age of hysteria and vocal competition. The true surgeon, who is an artist rather than a maniacal egoist, tends to have his real work, which one might reasonably imagine to be the practice of surgery, thrust into the background by an importunate and impatient public, medical and lay.

There is a satisfactory chapter on surgical technique. It is well known that many of the instruments described therein have been devised by the authors themselves. In fact, their whole system of operative gynaecology is somewhat loosely, though not infrequently, termed the "Bonney-Reverdin" technique by surgeons in general. The number of necessary assistants and accessories has perhaps been overstated. It may be wise to remind ourselves and others that a surgical operation is a serious affair, even to-day. But, unless he be particularly adaptable, the surgeon who is accustomed to operate amidst a plethora of skilled support must inevitably find himself at a loss when he is forced to function with the assistance of half-witted obstructionists in one of those ill-fitted pig-styes which are a disgrace to modern civilization. On the other hand, it is salutary to bear in mind that at least 90 per cent of the transactions of every surgical operation are conducted by Nature, and that all the king's horses and all the king's men failed to restore *per se* the anatomical relations of poor Humpty Dumpty.

We are glad to notice that dilatation of the cervix has been treated with respect. The potential dangers and risks have been emphasized; and the manner of dealing with various complications has been fully considered. The authors are always alive to the possibility of complications—unlike those gentlemen with convenient memories, who have never had any trouble after any operation. As an instance of this conscientious care, we may note the introduction of the "safety-bolt" suture and other details in the excellent description of Bonney's method of amputation of the cervix, wherein the dangers of secondary haemorrhage are rightly stressed. Unfortunately, many people refuse to realize that one of the most cautious surgeons is he who is continually aiming at perfect results. Caution does not necessarily imply a lack of the highest degree of skill and courage.

The limited value of curettage is again recorded; and we feel that it will be necessary to labour the obvious in this direction for many years to come, although, unhappily, curetting enthusiasts are unlikely to read a textbook of this class. We entirely concur in the opinion that "a pregnancy of over three months in duration is, as a rule, best removed by abdominal hysterotomy"; and one wonders how much longer intelligent laymen, legal experts, and a considerable section of the medical profession will continue to regard the evacuation of a uterus comparatively advanced in pregnancy as a matter of "simple curettage."

It is frankly impossible to imagine any further improvement upon the various methods of abdominal hysterectomy, sub-total, total, and radical,

that have been elaborated and graphically described by the authors. The relative merits of total and subtotal hysterectomy have been fairly stated, as have those of abdominal and vaginal hysterectomy. There has of late been a tendency to resuscitate and "stunt" the vaginal operation; and, indeed, it is invaluable under certain conditions. We are glad to observe that in the majority of cases Berkeley and Bonney favour the abdominal method of approach. Nevertheless, the operation of vaginal hysterectomy is clearly and adequately outlined, apart from a variety of minor modifications that have been introduced in the course of the recent revival.

In the chapter on Opening and Closing the Abdominal Cavity, a rubber "round-about" is advocated, to protect the edges of the abdominal wound. Is this really necessary? And may it and similar contraptions not determine unnecessary trauma? In our experience those surgeons, *caeteris paribus* (an important point!), who have been most energetic to protect the abdominal wall from infection have tended to court, via trauma, that very disaster which they have sought to avoid.

As we have anticipated, the surgical treatment of carcinoma of the cervix has been brilliantly described and illustrated, together with a full account of the indications, difficulties, after-care, and complications. The fanatical zeal with which certain gynaecologists have denounced Wertheim's operation in their advocacy of radio-therapeutic measures has always led us to suspect that their own surgical experience may not have been too happy: it is given to few individuals, even though they be members of a "scientific" profession, to apply a detached mind to the consideration of any problem in which they themselves are intimately concerned. On this account we cannot but regret that Berkeley and Bonney have been bold enough and honest enough to publish mortality figures that are undeniably high! The reason for this considerable death-rate is not far to seek. On the one hand, they have included all their earlier cases; and on the other hand it is well known that they have considerably tackled border-line and advanced cases which might have been left well alone by less enthusiastic and more selfish surgeons. There is another reason: they appear to have scorned the application of deep X-ray therapy as an accessory measure. On this account, each of their operations has necessarily been pursued to the uttermost limits; and the attendant risk has thereby been increased, in spite of their skill. We agree that it is somewhat unreasonable to apply *radium* to a case that is shortly afterwards to be subjected to a radical operation; but we do contend that deep X-ray therapy is an invaluable pre-operative and particularly post-operative accessory. We further submit that this combination determines a lower mortality rate and a higher percentage of cures.

At the outset of the chapter which deals with abdominal myomectomy, there is an excellent paragraph on the conservation of the uterus, in which it is well stated that "cure without deformity or loss of function must ever be surgery's highest ideal". We can only remark that, if it is all-important to conserve, whenever possible, a uterus that harbours fibroids, it is still more important to reduce the number of hysterectomies that are annually performed for functional menorrhagia, by taking advantage of recent advances in corpus luteum and anterior pituitary therapy—no longer a wild dream. In a later chapter abdominal hysterotomy and curettage are coun-

tenanced "to explore the uterine cavity in certain cases of uterine haemorrhage in young women in whom the cause of bleeding is obscure". Is it obscure, in the light of modern research? And is this strictly conservative surgery? It is true that the authors do not strongly advocate utriculoplasty in these cases; and for this attitude we venture to commend them, for surely the operation represents a physiological anachronism.

As regards Caesarean section, we do not like the outline of indications offered on account of pelvic contraction. Due attention is not paid to trial labour; yet it is well known that the very large majority of doubtful cases of disproportion undergo spontaneous labour when put to the test. Nature is considerably more successful in persuading a foetal head to enter the pelvic brim than the hand of the most expert obstetrician. Must all these doubtful cases be subjected to Caesarean section—of which we know the mortality risk to be in the neighbourhood of 1 per cent under the best conditions? The authors would appear to have considered the problem rather as a matter of pelvic inches than as one of relative measurement. Bonney's "lower segment" Caesarean section is a brilliant contribution to surgical technique; but it is not the operation to which the term is usually applied. It is performed before the onset of labour, or early in labour; and use is made of a special uterine compressor and Willett's scalp forceps. The "lower segment" operation, as generally understood and performed in cases of obstructed labour, is not adequately discussed; but perhaps this has been rightly relegated to textbooks which deal with obstetric procedures.

We entirely agree with the opinion that pre-sacral sympathectomy for dysmenorrhoea "should not be undertaken until all lesser means of alleviating the patient's sufferings have been tried and have failed"; but we are not so pessimistic as to believe that the operation in this country is "still on its trial".

Operations to remedy displacements of the genital canal are fully considered and very clearly depicted. Anatomists have always treated the female pelvic floor with scant courtesy, although it seems to us to be far more worthy of study than that of the male. This defect, however, has been remedied by gynaecologists in general, and by the present authors in particular. Their anatomical descriptions in this textbook are brief but perfectly clear. There is a very good diagram on p. 464; and the whole chapter is excellent. Manchester is apt to complain, somewhat unreasonably, Fothergill's operation is never performed in London. We trust that Manchester will approve of the modification herein so well described and illustrated, and that its citizens will appreciate the tribute paid to the memory of a very great gynaecologist and to his associates.

Operations upon the ovaries, broad ligament cysts, and uterine appendages, do not lend themselves to originality in the present state of our knowledge. We have nothing but praise for the manner in which they are treated. The same sentiment applies to the chapter on extra-uterine gestation and tumours complicating pregnancy.

We strongly endorse the opinion that the appendix should not be removed as a routine procedure in the course of gynaecological operations. There are chapters on enterectomy, colostomy, etc.—procedures which a gynaecological surgeon may be called upon to undertake *in medias res*; and

there is a whole chapter on abdomino-vaginal excision of the rectum, Bonney's modification of the method of Ernest Miles. There is also an excellent chapter on operation wounds of the bladder, ureter, and bowel.

The chapters on post-operative treatment and complications are among the best in the book; and many of us will consult them more or less surreptitiously from time to time. They show every evidence of detailed experience, clinical judgment, healthy self-criticism, and insight into human nature. As a rule, gynaecological surgery is, or ought to be, comparatively free from serious complications; since, apart from pulmonary embolus and the like, we deal with tangible factors, and the laws of cause and effect are upheld. Degrees of infection are usually calculable, and not variable as in intestinal surgery. In the main this is a great advantage, as we are enabled to anticipate and obviate complications with a measure of accuracy that is almost mathematical. The disadvantage, if any, lies in the fact that we can look back if ill befalls, and if we are afflicted with a surgical conscience and a memory for detail, we can place a self-condemnatory finger on the weak spot in the original proceedings. Happy is the gynaecologist of aloof mentality; but he is a bad surgeon. The authors are clearly interested in after-treatment; and indeed without this interest the practice of surgery is sterile and inhuman. They are also up to date, as instanced by the consideration of such therapeutic agents as acetyl-choline and prostigmine. It is difficult to imagine any post-operative problem that may have escaped thoughtful and respectful examination and solution in these pages.

The immediate and remote results of gynaecological operations are fairly stated. Statistics of this type are of limited value, as each unit represents such a great variety of factors. They are quoted and discussed *ad nauseam* by the Tadpoles and Tapers of surgery to the third place of decimals; but the wise man merely employs them to correct his own bias.

Lest it appear that we have been unduly critical here and there, we must re-emphasize the opinion that the main features of this great textbook are beyond criticism and beyond praise. It is a classical work; and it will be the mainstay of gynaecological surgery for years to come. Those of us who have had the privilege of first-hand acquaintance with the authors will realize how complementary they have been the one to the other in all their work. They have applied this ideal psychological combination to the great gain of an honourable profession and of the whole world. May their happy and productive association long continue.

Frank Cook.

"The Treatment of Common Female Ailments." By F. J. McCann, M.D., F.R.C.S., F.C.O.G., M.R.C.P. Pp. viii + 379. Edward Arnold and Co., London, 1934. Price 12s. 6d.

This book is intended specially for the general practitioner as a guide to the treatment of female pelvic ailments. In the new edition fresh chapters have been added, among others, on The Relation of the Endocrine Glands to the Genital Organs, The Climacteric, Gastro-Intestinal Complications of Female Ailments, The Prevention of Conception as a Cause of Female Ailments and Fertility and Sterility. The book is not a textbook in the ordinary

sense. It is rather a description under the different groups of gynaecological disease of the various alternative therapeutic methods—medical and surgical—which are available for the practitioner. Throughout it gives expression to the extensive experience of the author. In a book which is professedly intended to emphasize the personal views and practice of the writer the dogmatic statement is in general calculated to add to the vigour and value of the presentation. In many places in his dogmatism the author challenges much that is orthodox. Take, for example: "further, it is frequently advised that nothing should be done if symptoms are absent. To this I reply that sooner or later a backward displacement will cause symptoms, and that as a spontaneous cure in chronic cases is not be expected, the sooner the displacement is remedied the better for the patient."

James Young.

"Handbook of Gynaecology," third edition. By BETHEL SOLOMONS, B.A., M.D., F.R.C.P.I., F.C.O.G., M.R.I.A. Pp. xiv+368. Figs. 250. Size 5in. by 8in. Baillière, Tindall and Cox, London, 1934. Price 15s.

In the preparation of this new edition the author has carried out a complete revision of the text. The results of recent work on sex physiology are incorporated, and the present position of hormone therapy is described clearly and with commendable caution. The chapter on sterility has been rewritten, and the section on operations has been revised. There is a new chapter on Radium and X-rays in Gynaecology by Mr. Oliver Chance. The book is increased by over fifty pages.

Throughout the book the author has adopted a simple style of presentation which is usually clear and effective and, throughout, the aim has been to treat the subject in a manner which is essentially clinical with a minimum of reference to the associated pathological states. In the pursuance of this aim the briefness with which the pathology is handled sometimes leaves the descriptions somewhat vague and lacking in definition. In the chapter on retrodisplacement of the uterus, for example, the statement is made that "the first three symptoms (menorrhagia, metrorrhagia and leucorrhoea) cited are due to the endometritis following the displacement." The student is left to question how such a change in the position of the womb can produce an endometritis. In the discussion adenomyosis uteri, similarly, it is stated that "the main symptom is sudden violent bleeding, which is supposed to be caused by the kinking of the blood-vessels by the gland islands."

The volume is attractively prepared and the illustrations are numerous, well chosen, and clear.

James Young.

Biological Monographs and Manuals. No. 11. "Maternal Behaviour in the Rat." By BERTOLD P. WIESNER and NORAL M. SHEARD. Oliver and Boyd. Edinburgh: 1933.

THE present volume is so far removed from the sphere of practical obstetrics and gynaecology that only a brief account will be given. These biological

monographs have provided a series of very valuable books for the general biologist and the research worker generally, who wishes to obtain specialized knowledge concerning subjects rather outside his province. Thus earlier works include volumes on "The Pigmentary Effector System," "Statistical Methods for Research Workers," and "Reproduction in the Rabbit." The volume under review deals with maternal behaviour in the rat, and summarizes in a clear and lucid manner an astonishing amount of hard work and painstaking observation not only on the part of the authors, but of other workers in this field. Accounts of the maternal behaviour of the rat are given in such detail as to astonish those unaccustomed to this type of literature.

E. C. Dodds.

"Obstetrics and Gynaecology." Edited by A. H. CURTIS, M.D. W. B. Saunders & Co., Philadelphia.

THESE three volumes represent the first complete presentation of the subjects dealt with, emanating from America. They have the advantage of the editorship of Dr. A. H. Curtis, the Professor of Obstetrics and Gynaecology at the North-Western Medical School, Chicago, who has inspired the undertaking. Around him he has gathered a large number of contributors, all of whom have been selected as authorities in the various subjects allotted to them.

Dr. Franklin H. Morton, in the opening article, envisages the whole work as expressing "what America has to tell about obstetrics and diseases of women," but after perusal we feel bound to admit to an impression that in many departments America is repeating what has been told to her. Taking three articles at random we find on studying the references that, so far as concerns these three subjects, 78 per cent of the references are not of American origin. It is, however, meet that this should be so. The problems with which these volumes are concerned are international, and the authors are alive to any contribution to the vast subject which they present.

As is the case with all American scientific works, the publishers have done their part splendidly, and the general production of this "Obstetrics and Gynaecology" is excellent; printing, paper and illustrations being equally good.

The first volume opens with a masterly article entitled "Historical," by Dr. Irving S. Cutter, which is equal to anything which comes later and shows the work of an expert and scholarly historian at his best. We trust we will be forgiven the reflection that William Smellie is deserving of more extended reference than that which is accorded to him.

The sections dealing with the anatomy and physiology of the female generative tract are in every way worthy of the occasion, and that dealing with the morphology and physiology of pregnancy is illuminated by an outstanding contribution on the embryology of the genital tract from the pen of Dr. Arthur K. Hoff.

Most of the remainder of the first volume is taken up by the presentation of the subject of normal pregnancy, labour and the puerperium, with a curious lapse into abnormality when pyelitis of pregnancy is discussed; and the volume ends with chapters on the toxaemias of pregnancy, disturbances

due to diseases and abnormalities of the female genitalia, and upon spontaneous abortion and premature labour.

There must of necessity be overlapping of subject matter and a certain warring of styles in a composite book such as this, but the general impression is that the balance is well held and that Dr. de Lee and the late Dr. Whitridge Williams have completely moulded American obstetric thought to their teachings.

The second volume is devoted to the Pathology of Labour and Puerperium and Operative Obstetrics, after which Gynaecology proper takes the field and the modern knowledge of infective processes and tumours is collected and presented.

The article dealing with contracted pelvis is not worthy of the book, and future editions will probably contain a more extended survey of the subject from a clinical standpoint. The author of the article upon dystocia due to anomalies of the expulsive forces presents the contraction ring to his readers in a manner markedly at variance with the views held in this country. The subject of anaesthesia in labour is found discussed in that part of the volume dealing with anomalies of the passenger, and is closely followed by a description of the author's method of performing Caesarean section. In this article, incidentally, the author writes in the third person, the first person plural, and the first person singular in four consecutive paragraphs.

The pages dealing with haemorrhages are very good, and follow Professor de Lee's teaching throughout. Professor Watson has written a characteristic article upon puerperal sepsis, which, with Dr. Stander's article upon Caesarean section, Dr. Goodall's article upon tumours of the ovary, and the late Dr. Grave's contribution upon uterine myomata may be selected as the best parts of the volume. The beautiful drawings in the last article mentioned remind us once again of the great loss American gynaecology has suffered by Dr. Grave's death.

The third volume is devoted to the consideration of displacements and relaxations, disturbances of function, endocrines, special diseases and complications, and ends with a survey of certain special topics. There is an excellent article upon sterility and a contribution upon therapeutic abortion and sterilization which gives a sane and judicial outlook upon these subjects. It shows that in America, as here, professional opinion is not yet sufficiently crystallized to be able to lead the community usefully.

The section dealing with endocrines in Gynaecology and Obstetrics extends to nearly 100 pages and forms one of the most complete presentations of the present state of knowledge that we have read. The section on Ectopic Pregnancy, on the other hand, might with advantage have been much fuller. The subjects of pre-operative treatment, anaesthesia and post-operative management are handled with shrewd observation, and the final articles are concerned with the relations of general medicine to gynaecology and obstetrics.

In conclusion we desire to congratulate Dr. Curtis and his co-workers on the production of a very useful and impressive work.

J. Bright Banister.

Review of Current Literature.

THIS Review contains the lists of contents and abstracts of the more important articles from the following journals with which the "Journal of Obstetrics and Gynæcology of the British Empire" exchanges :—

British.—The Lancet; British Medical Journal; The Cancer Review :
Canadian.—The Canadian Medical Association Journal; Bulletin Médical de Quebec.
Australian.—Medical Journal of Australia; The Australian and New Zealand Journal of Surgery.
Indian.—The Calcutta Medical Journal.
American.—American Journal of Obstetrics and Gynecology; The Journal of the American Medical Association; Surgery, Gynecology and Obstetrics.
French.—La Gynécologie; Gynécologie et Obstétrique; Bulletin de la Société d'Obstétrique et de Gynécologie de Paris.
Belgian.—Bruxelles-Médical.
Italian.—Annali di Obstetrica e Ginecologia; Archivo di Obstetrica e Ginecologia.
German.—Archiv für Gynäkologie; Zeitschrift für Geburtshülfe und Gynäkologie; Zentralblatt für Gynäkologie; Monatsschrift für Geburtshülfe und Gynäkologie; Münchener Medizinsche Wochenschrift.
Scandinavian.—Acta Obstetrica Scandinavica.
South American.—Boletin de la Sociedad Obstetricia y Ginecologia de Buenos Ayres.
Japanese.—Japanese Journal of Obstetrics and Gynæcology.

The Review of Current Literature thus keeps the readers of the Journal in touch with current literature throughout the world. At the end of the year an Index of all the subjects contained in the articles of the above journals is printed. Arrangements are also made to include abstracts of important articles on border-line subjects, such as Physiology, Biology and Biochemistry.

LIST OF ABSTRACTORS.

London: J. BEATTIE, F.R.C.S.; A. C. BELL, F.R.C.S.; R. K. BOWES, F.R.C.S.; J. LYLE CAMERON, F.R.C.S.; R. L. DODDS, F.R.C.S.; R. C. LIGHTWOOD, M.D.; D. H. MACLEOD, F.R.C.S.; J. A. MOORE, M.B.; C. D. READ, F.R.C.S. (Edin.); F. ROQUES, F.R.C.S.; R. WINTERTON, M.D.
Huddersfield : W. E. CROWTHER, M.B.
Leeds : R. H. B. ADAMSON, M.D.
Liverpool: M. DATNOW, M.D.; P. MALPAS, F.R.C.S.
Glasgow: JANE H. FILSHILL; R. SHARMAN, M.D.; H. MACLENNAN, M.D.

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*A criticism of ante-natal work. A. J. Wrigley.

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Pregnancy diagnosis in theory and practice. J. M. Robson.

Psychological effect on hysterectomy. Victor Bonney. (Correspondence.)

Criticism of ante-natal work. A. S. Garden. (Correspondence.)

Prevention of puerperal sepsis. G. F. Gibberd. (Correspondence.)

June 23rd, 1934.

*Angular pregnancy. A clinical entity. J. M. Munro-Kerr and David Fyfe Anderson.

Psychological effect of hysterectomy. Marion Greaves. (Correspondence.)

Criticism of ante-natal work. Aleck Bourne. (Correspondence.)

Prevention of puerperal sepsis. Norman H. Joy and R. D. B. Wright. (Correspondence.)

June 30th, 1934.

The ante-natal use of quinine. F. W. Buddee.

Pregnancy diagnosis. P. M. Bishop. (Correspondence.)

Psychological effect of hysterectomy. S. Vatcher. (Correspondence.)

July 7th, 1934.

Severe menorrhagia due to chronic thrombocytopenic purpura cured by splenectomy. Stanley J. Hartfall and Carlton Oldfield.

July 14th, 1934.

*Full-time extra-uterine pregnancy with living child. W. Arkley Steel.

Spontaneous rupture of the uterus at the twenty-fourth week. J. R. Campbell Canney.

The ante-natal use of quinine. Douglas A. Mitchell. (Correspondence.)

July 28th, 1934.

Principles of gynaecology. W. Blair-Bell. (Correspondence.)

A case of angular pregnancy. William H. Gossip. (Correspondence.)

August 11th, 1934.

Splenectomy for menorrhagia in purpura haemorrhagica. Bernard Myers. (Correspondence.)

August 4th, 1934.

Are we satisfied with the results of ante-natal care? John S. Fairbairn, F. J. Browne, Ethel Cassie, and George F. Buchan.

Concurrent extra-uterine and intra-uterine gestation. H. Grey Massiah.

Maternal mortality in Maoris. Violet E. Hastings. (Correspondence.)

A Criticism of Ante-natal Work.

Ante-natal supervison dates from about 1902. It is disappointing that when considering the figures of the national maternal mortality, no impression on these figures has been made, and, indeed, in the last year or two the mortality has shown a slight rise. The author, in attempting to show the effect of ante-natal supervision, carried out as it is at the present time, deals with some of the more important complications of pregnancy. Ante-natal supervision has failed to reduce the maternal mortality from eclampsia and allied conditions. Ante-natal supervision has resulted in the erroneous diagnosis of minor degrees of disproportion in women in whom it did not exist. Unnecessary interference has resulted, such as the induction of premature labour and Caesarean section, with an infantile mortality of 10 per cent. External cephalic version, when performed under an anaesthetic, may be a dangerous procedure. At one institution where version under anaesthesia had been performed with an accompanying stillbirth rate of 13 per cent, some 70 breech cases were delivered in the last five years with an infantile mortality of only 10 per cent. In conclusion, the author shows that ante-natal supervision cannot accomplish all or even half of what has been claimed for it. The search for the abnormal has masked the preservation of the normal.

Angular Pregnancy: A Clinical Entity.

Two cases of angular pregnancy are described. Both were admitted to the same hospital within twenty-four hours of each other. Professor Munro-Kerr describes a further case which he had reported many years ago. By angular pregnancy is meant a condition in which the zygote becomes implanted in the angle or cornu of the uterus. It is quite distinct from the typical interstitial pregnancy. Pain in these cases may be very severe, and abortion is common. The outline of the uterine distension is characteristic. These cases usually attract attention between the twelfth and twentieth weeks of pregnancy.

Full-time Extra-uterine Pregnancy with Living Child.

A case of full-time extra-uterine pregnancy is described. There was a history of acute severe pain when about 20 weeks pregnant. At examination the fundus uteri could not be defined apart from the centrally placed tumour. Later external version was performed at term under anaesthesia after which the patient's condition was seen to become bad. At laparatomy the abdomen was found to be full of blood and the sac was ruptured. A live child was extracted. The child lived for only 12 hours, but the mother made a good recovery.

D. H. MacLeod.

The Lancet.

June 2nd, 1934.

*The possible role of the foetus in labour. R. A. Gibbons.

June 16th, 1934.

*A new technique for the self administration of gas-air analgesia in labour. R. J. Minnitt.

July 7th, 1934.

The dangerous multipara. Bethel Solomons.

Cyclopropane anaesthesia in obstetrics. Wesley Bourne.

Suppurative ovaritis following mumps. J. B. McKinney, H. Hilton Stewart, and H. J. McClure.

July 14th, 1934.

Cyst formation in ovarian grafts. J. S. Hall.

July 21st, 1934.

Radiographic evidence of live birth. Miren Hajkis.

August 11th, 1934.

The toxaemias of pregnancy: (I) Clinical and biochemical investigation. Dame Louise McIlroy.

August 18th, 1934.

The toxaemias of pregnancy, (II). Dame Louise McIlroy.

*The fate of the follicular hormone in the living body. Professor B. Zondek.

September 8th, 1934.

Extraperitoneal ovarian graft cyst. H. H. Kidd. (Correspondence.)

The Possible Role of the Foetus in Labour.

The author believes that the onset of labour is due to an oxytocic substance which is poured into the maternal circulation. The ovaries and pituitary gland play no part in this. Normal labour at term has followed double oöphorectomy at six weeks after conception in a woman, and in experimental mammals in which the pituitary gland was removed. The blood from the umbilical cord differs from that of the maternal circulation. It has been shown that blood taken from the umbilical cord contains substances which promote the activity of the uterus of a guinea-pig to a far greater extent than that of the mother. The author believes that in the future more delicate biochemical tests may be forthcoming which will throw new light upon the research, and that more attention should be paid to the foetus.

A New Technique for the Self-administration of Gas-air Analgesia in Labour.

The author describes an apparently satisfactory method for the self-administration of a mixture of gas and air. The apparatus, which is an adaptation of a McKessow oxygen therapy apparatus, is described. Scientific work has been carried out to show there is no danger to the mother or

child, and the average length of the second stage of labour is within normal limits. The relief from pain and distress were good, and there were only nine per cent of failures. The advantage of this method is analgesia without loss of consciousness. It is only intended for use in normal labour, and is not applicable for the application of the forceps and other operative procedures.

THE FATE OF FOLLICULAR HORMONE IN THE LIVING BODY.

The paper is a brief report of experiments dealing with the fate of oestrogenic hormone in the living body. It was found that after the administration of large doses of hormone very little could be recovered from the urine. In order to investigate this, infantile rats, which had been given folliculin subcutaneously, were analysed. It was discovered that when three hours had elapsed after giving folliculin only very small quantities could be demonstrated in the animal. This is surprising when it is remembered that the biological effect takes some days to appear. It is obvious from the above experiments that folliculin is not stored in the body, and further experiments have shown that the hormone becomes inactivated. The folliculin becomes fixed to the cell walls by absorption, especially to the cells of striped muscle.

D. H. MacLeod.

The Biochemical Journal.

Vol. xxviii, No. 3, 1934.

*Changes in serum-calcium and magnesium and in the inorganic phosphorus of the blood of cows at calving, and of the calf during early life. W. M. Allcroft and W. Godden.

No. 4.

*Rapid method of determining total protein and non-protein nitrogen in human milk and cow's milk. L. D. Scott.

CHANGES IN SERUM-CALCIUM AND MAGNESIUM.

There is a tendency for the serum-magnesium level to be high just before and within 24 hours after calving. In general the quantity of serum-magnesium varies with that of serum-calcium. Calves at birth and for the first eight weeks of life show a higher level of serum-calcium and blood inorganic phosphorus than the normal for their dams. The serum-magnesium level in the calf at birth is lower than that of the dam, but reaches normal in about three weeks.

TOTAL PROTEIN DETERMINATION.

A quantitative method is described for the routine estimation of total protein and non-protein nitrogen in milk. Zinc hydroxide is used as the precipitant of the protein.

J. A. Moore.

The Journal of Physiology.

Vol. lxxxii, No. 2, 1934.

Blood volume and oxygen capacity of the foetal blood of the goat. R. H. Elliot, F. G. Hall, and S. tS. G. Huggell.

No. 4.

*Output of foetal heart in the goat. J. Barcroft, L. B. Flexner, and T. McClurkin.

OUTPUT OF THE FOETAL HEART IN THE GOAT.

The quantity of blood flowing through the foetal heart was estimated at various stages of gestation. It was found that the ratio of the blood flow through the heart to the body-weight varied little. The oxygen used by the foetus also remained constant at about 0.0025 ± 0.001 per gramme per minute and increased four or five times after birth. The quantity of blood flowing through the foetal heart relative to the body-weight is the same before and after birth.

J. A. Moore.

Canadian Medical Journal

Vol. xxxi, No. 3, September 1934.

*Spinelli operation followed by pregnancy and labour. W. Pelton Tew.

SPINELLI OPERATION FOLLOWED BY PREGNANCY AND LABOUR.

The author refers to the work of Miller, who collected from the literature 55 cases of inversion of the uterus followed by pregnancy. Sixteen patients were primiparae, 21 multiparae. The inversion was immediately corrected in 15 cases; the average duration of the inversion for the whole group was 33 days; the longest interval was 12 months. Replacement occurred spontaneously in eight cases; was effected manually in 25; by operation in 22. Inversion recurred 11 times in 25 cases corrected manually; there was no recurrence in subsequent pregnancies among the 22 cases corrected by operation; subsequent abortions occurred three times. Adherent placenta occurred in 40 per cent of the cases corrected manually and in 18 per cent of the cases corrected by operation. Of the 22 cases corrected by operation, 29 confinements were reported afterwards. Uterine rupture did not occur in any case.

The author reports a case. His patient, aged 29, had had two normal deliveries; the third labour lasted four hours. The placenta was found to be adherent, but appeared to have been removed manually, during the process of which a mass, thought to be a pedunculated fibroid, was felt in the uterus attached to the posterior wall of the fundus. Ergot and pituitrin were given after the labour to arrest haemorrhage, which was free. There was no complaint of pain. Five hours after delivery the pulse-rate was weak,

haemorrhage had stopped within 12 hours, and the patient left hospital on the twelfth day with a normal temperature and a pulse-rate of 90. During the lying-in period the temperature was 100°F. and the pulse-rate also 100.

The patient noticed a mass protruding from the vagina when standing. This mass decreased in size except during menstruation, when it again protruded. When examined the patient was menstruating and the uterus was protruding through the vulval orifice. The everted surface could be seen weeping droplets of blood. The inversion had lasted for two years. Spinelli's operation was performed, and a good recovery followed. Two years later pregnancy resulted, labour lasted four hours, and delivery was spontaneous; the placenta was delivered by Crede's method. When examined subsequently the patient appeared to be normal in every way.

J. Lyle Cameron.

Bulletin de la Societe Medicale des Hopitaux Universitaires de Quebec

No. 9, September 1934.

*Pseudo-chorio-adenoma of Ewing. J. Caouette and O. Grant.

PSEUDO-CHORIO-ADENOMA OF EWING.

The case reported was that of a patient aged 23, who had had two normal children and one miscarriage. The fourth pregnancy was attended by intractable vomiting and albuminuria. At the twelfth week there was a severe haemorrhage and the patient expelled a vesicular mole. Examination, subsequently made because of continued bleeding, revealed the presence of bilateral painless ovarian tumours. These were removed, the uterus being conserved. Eight months later subtotal hysterectomy was performed on account of persistent haemorrhage. There were three small nodules in the uterine muscle. On microscopical examination they were seen to be composed of placental tissue in which there were foci of necrosis and haemorrhage. The chorionic villi were fibrosed and the epithelial elements did not show proliferation.

The author refers to the work of Marchand, who in 1898 described the placental origin of chorionic epithelioma. He classified placental tumours under two heads: (1) Atypical tumours, in which Langhans's cells have not undergone marked proliferation, the syncitium has become invaded by leucocytes and are becoming organized, and (2) Typical tumours, in which there is great proliferation of Langhans's cells, together with large masses of syncitium and invasion of the capillary vessels; the latter type is extremely malignant.

The author considers Ewing's classification more descriptive of clinical conditions. Ewing describes three types of placental tumours.

(1) *Chorionic adenoma* which usually follows hydatidiform mole. The uterus is greatly enlarged due to increase of the chorionic elements. There is an attendant increase of fibrous tissue. Secondary growths are quite exceptional.

(2) *Chorionic carcinoma*, perhaps the most terrible of all cancers. It frequently develops after a normal confinement. Metastases occur early. This is similar to the first type of tumour, except that there is no formation of fibrous tissue, and proliferation of the syncitium and Langhans's cells is extreme.

(3) *Syncitial endometritis.* This is an inflammatory phenomenon rather than a new growth. It is characterized by uterine hypertrophy and the presence of syncitial elements distributed throughout the endometrium; there is a marked tendency to retrogression.

The author urges the importance of bearing in mind the possibility of these growths following the expulsion of a hydatidiform mole; in such cases he advises exploration of the uterine cavity with the finger; the curette is dangerous because of the liability to perforation. The patient must be kept under observation for a considerable time afterwards.

Should metrorrhagia begin one or two months after the expulsion of the mole, exploratory curettage should be performed, and should this fail to arrest the bleeding, hysterectomy is indicated, because of the possibility of one of these growths being present and having escaped detection by the curettage. The Aschheim-Zondek test, or Brouha's test, should be made several weeks after the expulsion. When these are positive it is an indication that there is a metastatic growth present. Frequently the secondary tumours disappear after the primary growth has been removed.

There is no urgent need to remove the bilateral luteal cysts of the ovaries, which frequently accompany hydatidiform mole. They may vary in size from that of a hazel nut to that of a foetal head. Should they persist, however, after more than two months from the time of expulsion, they are prognostic of the presence of chorionic epithelioma of the uterus and total hysterectomy with bilateral oöphorectomy is indicated.

J. Lyle Cameron.

Medical Journal of Australia.

Vol. xi, No. 2, July 14th, 1934.

Disorders of the menopause. James Buchanan.

Case of double uterus with absence of right kidney and ureter. H. A. Ridler.

Vol. xi, No. 6, August 11th, 1934.

*Radon in the treatment of cervical carcinoma. W. A. Cuscaden.

*Case of puerperal inversion and prolapse. Percy Brett.

Vol. xi, No. 7, August 18th, 1934.

The hormonal control of the female reproductive system. R. Marshall Allen.

*A radium colpostat. Sylvia Bray.

Vol. xi, No. 8, August 25th, 1934.

*Case of ovarian haemorrhage. R. Errol Maffey.

Vol. xi, No. 10, September 8th, 1934.

Ovarian haemorrhage. Rowland C. Edwards. (Correspondence.)

REVIEW OF CURRENT LITERATURE

Vol. 11, No. 12, September 22nd, 1934.

Ovarian haemorrhage. Clive Greer. (Correspondence.)

*Treatment of ruptured tubal gestation. A. R. H. Duggan.

Vol. xi, No. 13, September 29th, 1934.

*Trichomonas vaginalis in relation to leucorrhoea. C. S. Graham and E. Collins.

Vol. xi, No. 14, October 6th, 1934.

Uterine fibroid inversion of uterus. H. A. Ridler.

RADON IN THE TREATMENT OF CERVICAL CARCINOMA.

Six tubes are used, each containing 12 millicuries, screened by a gold shield equivalent to 2.5 millimetres of platinum. After dilating the cervical canal two tubes are inserted into the uterus *in tandem*. A special square vulcanite applicator is used for the fornices. The posterior part has a shield of lead, six millimetres thick, to protect the rectum. The radon is left in place eight days. Two to three months later radon is implanted into the broad ligaments. A table of results is given.

CASE OF PUERPERAL INVERSION AND PROLAPSE OF THE UTERUS WITH SPONTANEOUS EVOLUTION.

The patient was admitted to hospital with inversion and prolapse of the uterus. Shock was treated and later the prolapse was reduced, but the inversion could not be corrected. The patient returned home after four weeks in hospital, with the uterus still inverted although involuted. Four weeks later, when she was admitted to hospital, spontaneous evolution had taken place.

A RADIUM COLPOSTAT.

This consists of two rubber corks with a hole bored through each to hold the radium. The corks are held together by a piece of copper wire, four to five inches long, the ends of which are bent round the middle of each cork. The wire is covered by rubber tubing and the corks by rubber dam.

A CASE OF OVARIAN HAEMORRHAGE.

The patient was aged 29. Her last normal period began on December 30th, 1933, and lasted four or five days. The next occurred on February 1st, was more profuse than usual and lasted seven days, followed, after an interval of two days, by a reappearance of the flow, less in amount which had lasted till the consultation on March 19th. Since the reappearance of the vaginal haemorrhage she had had constant lower abdominal pain. There was tenderness over the lower abdomen, worse in the left iliac fossa. The temperature was normal, the pulse-rate 86, respiration-rate 22. There was tenderness in all fornices and a small tender lump in the left broad ligament. She was sent to hospital for observation as a case of leaking tubal pregnancy. Two days later her temperature rose to 99.4°F., the pulse-rate to 120, and the lower abdominal pain increased. Two days after this the abdomen was opened, after curettage had shown nothing abnormal in the uterine cavity.

A small amount of free fluid was found in the peritoneal cavity. The right ovary was larger than the left, and a mass of blood-clot, about the size of an ovary, was adherent to it. The ovary and clot were removed. Convalescence was uneventful. The histological examination showed organizing blood-clot. The ovary showed a large number of cysts of various sizes, an adenomatous condition. There was no evidence of pregnancy or malignancy.

TREATMENT OF RUPTURED TUBAL GESTATION.

The author advocates immediate operation which has a mortality of less than 10 per cent as opposed to mortalities given by various authors of from 17 per cent to 86 per cent for expectant treatment. He advises pre-operative blood-transfusion in shocked patients if a donor is available, or failing blood-transfusion, autotransfusion or the infusion of intravenous saline with six per cent of glucose.

TRICHOMONAS VAGINALIS IN RELATION TO LEUCORRHOEA.

Trichomonas causes a leucorrhoea which has a disagreeable odour and is irritating to the skin. It is often bubbly and noticeably free from mucus. The parts become red and swollen and may show small ulcers. An erosion is often present. The vaginal walls show red, tender spots, which bleed easily. Vaginitis associated with trichomonas may complicate other gynaecological conditions. It is a frequent cause of leucorrhoea in virgins. The percentage of cases of leucorrhoea due to trichomonas is variously given by different observers as 28 per cent to 68 per cent. The authors found in their practice 14 cases out of a consecutive series of 49 adults suffering from leucorrhoea. Five of these cases were associated with some other gynaecological condition. The diagnosis has to be made from gonorrhoea. It may be associated with gonorrhoea. Serological and culture tests should be made as well as routine smears. A loop of material is mixed with warm saline and examined as soon as possible under a coverslip with the high power. The organisms remain active for about 15 minutes.

When the preparation is to be stained the organisms must be killed and fixed rapidly. The organisms have little resistance to antiseptics. The difficulty in treatment is to get into the crevices of the vagina. The prognosis is good, most cases clearing up after a short course of treatment.

W. R. Winterton.

The Calcutta Medical Journal.

Vol. xxviii, No. 12, June 1934.

Concealed haemorrhage in the early months of pregnancy. Sudhangsy Kumar Ghosh.

Vol. xxix, No. 1, July 1934.

*Glucose and calcium therapy in eclampsia. M. N. Sarkar.

A case of lympho-granulomatosis venerea or esthiomene vulvae. R. N. Ray.

GLUCOSE AND CALCIUM THERAPY IN ECLAMPSIA.

During the 10-year period 1923 to 1933, 649 eclamptics were admitted to the Eden Hospital, Calcutta, and the mortality was 38.5 per cent. Since

1932 the author has treated 78 cases by a new technique with a mortality of 7.6 per cent. The treatment involves the intravenous administration of 50 per cent glucose, and the intramuscular injection of 10 per cent calcium gluconate, but the treatment also includes the giving of morphia, intestinal wash-outs, and venesection.

A. C. Bell.

The American Journal of Obstetrics and Gynecology.

Vol. xxvii, No. 4.

Application of endocrinology to gynaecological problems. E. Novak.
Effect of changes in the amount of protein upon pregnancy and lactation. D. Macomber.
Effect of pregnancy on the organ weights of the albino rat. M. Abramsow.
Diffusable serum calcium in pregnancy. H. O. Nicholas, H. W. Johnson, and R. A. Johnston.
Variations in serum calcium and phosphorus during pregnancy. J. W. Mull and A. H. Bill.
*Primary breech presentations. D. E. Carmell and S. M. Dodek.
*Cardiac disease in pregnancy. H. J. Stander.
*Foetal mortality in contracted pelvis with prolonged labour and delivery through the birth canal. C. H. Peckham and K. Kuder.
Effect of pregnancy upon the ureters of common animals. W. F. Mengert.
Lesions of 1,500 placentae considered from a clinical point of view. H. F. Trant and A. Kuder.
*Cause of the onset of labour. J. T. Witherspoon.
Some attempts to influence the menstrual cycle in the monkey. C. G. Hartman.
Effect of jaundice on the vaginal smear picture and pregnancy of the rat. J. D. Greaves and C. L. A. Schnirdt.
*Deliberate rupture of the membranes early in labour. A. G. King.
Smallpox vaccination of the newborn. L. Isaac.
An anatomical study of a mammary gland 24 hours post-partum. I. A. Korneke.
Cystic schwannoma of the sacral plexus. R. T. Frank.
Brenner tumour of the ovary. S. A. Wolfe and S. Kaminester.
Acute renal failure complicating pregnancy. I. J. Strumpf.
Three cases of primary carcinoma of the female uretha treated with radium. L. A. Pomeroy.
Intrapartum gas bacillus infection. A. A. Marchetti.
Biopsy specimens of the endometrium. P. E. Hoffmann.
Case of spondylolisthesis. H. C. Williamson.
Carcinoma of cervix uteri with complete procidentia. W. F. Boukalik.
Dystocia following cervical amputation. H. C. Hesseltine.
An umbilical cord clamp. H. F. Kane.
Selected Abstracts.

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Vol. xxvii, No. 5.

*Leucoplakia cervicis uteri and early carcinoma. J. Hofbaner.
Pelvic oedema, diapedesis, and rhexis. J. R. Goodall.
An anatomical and clinical study of a thoracopagus monster delivered alive at full time. C. C. Shaw, B. B. Brumbagh, and M. A. Novey.
*Analytical study of the results of operations on the cervix uteri with special reference to strictures. E. A. Bullard.
*Variations of serum calcium and phosphorus during pregnancy. J. W. Mull and F. M. Kinney.
Posture and dysmenorrhoea. N. F. Miller.
X-ray cephalometry. S. Hanson.
*Relation between the early and late toxaemias of pregnancy. J. V. Missett.
Routine induction of labour at term. S. M. Stern.
Döderlein bacillus. Cultural and serological studies. C. P. Brown and E. Redowitz.
Experimental ligamentous relaxation in the guinea-pig's pelvis. W. T. Pommereuke.
*Placenta praevia. R. A. Wilson.
The use of dilaudid-scopolamine in obstetrics. W. A. Ruch.
Predicting the sex of the unborn child. E. F. Daily.
The impermeability of the placenta to prolan B. S. D. Soule.
Racial, geographical, annual, and seasonal variations in birth weights. L. Bivings.
Some observations on the rupture of the Graafian follicles in rabbits. J. T. Smith.
Hypertension six weeks post-partum in apparently normal patients. M. J. Stout.
Meconium peritonitis following spontaneous intra-uterine perforations of jejunum. B. Markolitz and Ralph Loar.
Tuberculosis of cervix uteri B. P. Watson.
Temporary surgical sterilization with subsequent pregnancy. A. H. Aldridge.
Gonorrhoeal infection during pregnancy associated with trichomonas vaginalis infestation. J. B. Berustine.
A defeminizing tumour. G. W. Phelan.
Pyometra following application of radium for carcinoma of the cervix. Aaron Hirsch.
Pyelitis in pregnancy. H. J. Stander.
An abdominal pregnancy near term, with successful termination, retained placenta, and observations on the post-partum excretion of prolan. H. H. Ware, and R. J. Main.
Gas-bacillus infection of the uterus. C. G. Collins and S. H. Wills.
Spontaneous rupture of the uterus. E. G. Waters.
Aneurysm of the internal iliac artery complicating pregnancy. T. K. Brown and S. D. Soule.
Volvulus complicating pregnancy. G. Kornfeld and I. Daichman.
Traumatic utero-intestinal fistula. F. C. Holden.
Pyometra of cervical stump in a case of arthritis. D. N. Barrows.

Sterilization by transplanting the uterine end of the Fallopian tubes. J. M. Slemons.
Plant-Vincent's infection of the vagina. E. R. Muntz.
Pocket implantation of the round ligaments. C. W. Doughtie.
Intrapartum rupture of the umbilical cord. N. B. Sackett.
Chorion-epithelioma, treated with radium followed by hysterectomy. R. M. Beach.
A case of oligohydramnios. S. B. Schenck.
Puerperal gangrene of the extremities. J. H. Cutchin.
Selected Abstracts—Artificial start of labour.

Vol. xxvii, No. 6.

*The importance of proper nomenclature in puerperal sepsis. A. F. Lash and E. J. De Costa.
Calcium deficiency in pregnancy and lactation. A. M. Mendenhall and J. C. Drake.
An interpretation of weight changes during pregnancy. H. H. Cummings.
Mild symptoms from rupture of follicular cyst or corpus luteum. J. P. Pratt.
Krukenberg tumours of the ovary. J. C. Masson.
*The constitutional origin of cerebral disease in the newborn. W. R. Shannon.
Posterior vaginal hernia. W. T. Black.
Haemoperitoneum resulting from hepatic birth traumatism. G. Rogers.
Parasacral anaesthesia in obstetrics. Beatrice E. Tucker and H. B. W. Benaron.
Experimental studies of puerperal infection. C. C. Torrance.
The anatomy and histology of placental circulation. P. J. Kearns.
An evaluation of maternal nitrogen and mineral needs during embryonic and infantile development. I. G. Macy and Helen A. Hunscher.
Observations on 101 cases of placenta praevia delivered by abdominal Caesarean section. I. A. Siegel.
Neoskiodan in amniography. E. L. Cornell and J. T. Case.
Rhabdomyoma of the hymen, with the report of a case in a child. A. C. Edwards and A. L. Richardson.
Roentgenographic diagnosis of anencephalus, with a report of five cases. T. B. Weinberg.
Krukenburg tumour of the ovary. M. V. Armstrong and S. A. Wolfe.
Prolapsus uteri near term. W. B. Serbin.
Accidental infection of the utero-ovarian venous system during lipiodol utero-salpingography. W. A. Coventry.
Rupture of uterus through a Caesarean scar after two normal deliveries following a classical Caesarean section. H. W. Yates and H. J. Rezanka.
*Copper ionization for the treatment of leucorrhoea in virgins. D. W. Tovey.
Sarcoma arising in an ovarian fibroma. C. G. Johnson and S. H. Wills.
*A vaginal stethoscope for use in locating a placenta in the lower uterine segment. C. M. Turman.
Special article—Eugenic sterilization. L. A. Emge.
Society transactions.
Book reviews.

Vol. xxviii, No. 1.

*Urological complications following pelvic irradiation. H. S. Everett.
*The value of hormonal study in the diagnosis of chorion-epithelioma. R. A. Kimbrough.
*Cancer of the cervical stump following subtotal hysterectomy. E. von Graff.
Premature separation of the placenta, with special reference to the aetiology of placental lesions. T. L. Montgomery.
Squamous cell epitheliomata in dermoid cysts of the ovary. V. S. Counseller and W. L. A. Wellbrock.
Menopausal symptoms and ovarian function following hysterectomy. A. B. Tamis.
Acute yellow atrophy of the liver in pregnancy. H. J. Stander and J. F. Cadden.
The distribution of congenital malformations in the United States. W. F. Peterson.
Foetal death from placenta circumvallata. J. E. Hobbs and P. R. Rollins.
*The effects of chloral hydrate on the maternal and foetal organisms from the standpoint of experimental study. R. E. Campbell.
Blood in the cerebrospinal fluid of the newborn. L. H. Smith.
An analysis of 84 cases of placenta praevia. J. Binder.
Sterilization of the female by coagulation of the uterine cornu. M. N. Hyams.
Obstetric analgesia. I. Daichman, G. Kornfeld, and M. M. Shir.
The use of dial in labour. C. H. Birnberg and S. H. Livingstone.
One hundred and thirty-four consecutive Caesarean sections without maternal mortality. W. F. Seeley.
*Malignancy in cervical polyps. F. S. Fetterman.
Diagnostic value of posterior colpotomy or needle puncture in ectopic pregnancy. H. S. Bush.
Twin abdominal pregnancy. C. B. Lull and J. B. Bernstine.
Uterus didelphys with full-time pregnancy in one uterus and fibroids in the other. M. J. Abramson.
*An endometrial theory of ectopic pregnancy and an intraligamentous pregnancy at six months. S. B. Schenck and J. M. Frankel.
Successful removal of an ovarian cyst weighing 75 pounds. R. J. Crossen and S. D. Soule.
Special Article—Breech deliveries.
Book reviews.

PRIMARY BREECH PRESENTATION.

After giving a short account of recent papers on this obstetric abnormality the authors report a series of 550 cases, an incidence of 3.4 per cent of all deliveries. There were three maternal deaths (0.55 per cent) and 39 mothers were reported as morbid (7.1 per cent). There was a gross foetal mortality of 19.2 per cent and a corrected mortality of six per cent. Five hundred and thirty were delivered by extraction, mainly as double footlings, but a few as single footling, or as frank breech, 13 by Caesarean section, and seven spontaneously. A description of the method of extraction is given; the

authors stress the importance of awaiting full dilatation of the cervix, of bringing down the legs and extracting before impaction, of avoiding dangerous traction, and undue haste or rough manipulations. While considering the full-time deaths the authors come to the conclusion that the mortality is considerably higher in primiparae; this opinion is in conflict with that of Caldwell and Studdeford, who believe there is a greater risk in multiparae. The position of the child did not affect the foetal deaths but they found that premature rupture of the membranes had a decided influence on the mortality. The authors advocate the more frequent use of external cephalic version as the foetal mortality and morbidity is hgher in breech than in any other presentation, and the use of Caesarean section in elderly primiparae complicated by this presentation.

Cardiac Disease in Pregnancy.

The author describes the normal cardiac output as increasing from the start of the fourth month until term, when it is about 50 per cent above the normal in the non-pregnant state. Labour still further increases this output above the value at term. Eighty-one pregnant patients suffering from heart disease were investigated, an incidence of 4.15 per cent of all cases. One mother died before delivery two and a half hours after admission, giving a mortality of 1.37 per cent. The cases were placed in one of three groups;—(*a*) With a cardiac lesion but able to stand the usual strain of everyday life without limiting their activities, (*b*) cases in which cardiac embarrassment occurred after exertion, (*c*) cases showing definite signs of failure of compensation. He recommends the careful investigation of cases in hospital, even of the first group, so that a true value of the working capacity of the heart can be estimated. He suggests that cases in group 1 can be allowed to go to term with a spontaneous delivery under anaesthesia, cases in group 2 should be watched even more carefully and the second stage abolished by the use of the forceps, and cases in group 3 should be delivered as soon as the acute failure has been overcome, at whatever stage it may be, and tubal sterilization carried out to prevent further pregnancies.

Foetal Mortality in Contracted Pelvis with Prolonged Labour and Delivery through the Birth Canal.

As a very exact clinical judgment is needed to predict a safe delivery of a child through a slightly contracted pelvis, the authors investigated the results to the child in 442 cases with contracted pelvis in which the delivery had occurred through the birth canal after a labour lasting for more than 30 hours. There was a gross foetal mortality of 19.23, and a corrected mortality of 13.56 per cent. Most of the pelves were of the generally contracted type, and yet the corrected foetal mortality was much greater in the flat and rachitic type than in the generally contracted type. Nearly half of the total cases were terminated by some operative measure and in 5.5 per cent (24 cases) craniotomy had to be performed. With spontaneous delivery the corrected mortality was 2.62 per cent, whereas in operative delivery it was 27.17 per cent, with the highest

percentage after breech extraction. The authors are of the opinion that version with breech extraction or breech extraction alone should be avoided in all cases of contracted pelvis because of this high mortality. The mortality rate with the forceps delivery was 7.19 per cent as compared with breech extraction of 38.46 per cent. The mortality also varied directly with the weight of the child.

THE CAUSE OF THE ONSET OF LABOUR.

After enumerating eight theories which have been advanced as possible causes of the onset of labour, Witherspoon gives an account of the theories and experiments of various authors in the field of hormonal causes. It has been suggested that at or near term the corpus luteum no longer exerts an inhibitive action on the formation of oestrin and that this substance, being in excess in the blood and placenta, stimulates the posterior pituitary gland to secrete an oxytōxic substance. Other authors found by their experiments that the uterine muscle was probably made more sensitive to the pituitary hormone near term by the withdrawal of the action of the corpus luteum. Forty-five women at term were treated by the author with varying doses of various substances containing oestrin, including the hypodermic injection of 25 cubic centimetres of whole blood obtained from a woman hard in labour. Of this number only 11 were delivered within 36 hours. He comes to the conclusion that in his series no case was made out for the hormonal theory of the cause of the onset of labour, and that as yet this form of treatment was of no clinical value for the induction of premature labour.

DELIBERATE RUPTURE OF THE MEMBRANES EARLY IN LABOUR.

After discussing the old and the new theories with regard to the importance of the bag of waters in labour, King describes his findings in 200 cases in which the membranes were deliberately ruptured. Only completely normal cases were included in this number—premature labour, induced labour, contracted pelvis, haemorrhage, abnormal presentations, etc. were all excluded. He controlled these by another exactly similar 200 cases in which the membranes were left intact. Also 100 similar cases of spontaneous rupture of the membranes within 24 hours before the onset of labour were added for comparison. As the exact onset of labour is often indefinite, he classified his cases into two-fingers or three-fingers dilatation when first seen. He found that the average length of labour was shortened from 6.5 hours (primiparae) and 5 hours (multiparae) to 4.6 hours and 3.3 hours respectively at two-fingers dilatation. At three-fingers dilatation the average length was reduced from 4.9 and 3.6 hours to 3.3 and 2.2 hours. Thus he shortened labour by about a third of the time. No increase in foetal mortality occurred, and it was also found that the infection and interference rates were decreased by one-third.

LEUCOPLAKIA CERVICIS UTERI AND EARLY CARCINOMA.

Hofbauer quotes Hinselman and v. Franque, who report that all their six cases of leucoplakia of the cervix, watched for a sufficient number of

years, have developed cancer, and that every cervical carcinoma originates in a leucoplakic patch. Hinselman also claims that he has found 160 cases of leucoplakia with the help of his colposcope. Hofbauer describes the miscroscopical features of the lesion as follows:—(1) Greater density and numbers of cells which take on a deeper strain; (2) conspicuous proliferation of the cells in the basal portion of the stratum mucosum; (3) an increased irregularity in shape of the elements of the basal zone, not infrequently associated with a well-defined sub-epithelial round cell infiltration.

Atypical and irregular downgrowths of masses of abnormal epithelium into the stroma are also described, making up much the same picture as that of early malignancy but without the break in the boundary of the basement membrane.

Because of the recent association of overactivity of the anterior pituitary and overgrowth of the mucous membrane of the female generative tract, the author sought to obtain evidence of hyperplasia of the squamous covering the vaginal portion of the cervix after transplantation of the peripheral parts of the anterior pituitary into the mature guinea-pig. Remarkable development of epithelial prolongations into the connective tissues was obtained, closely resembling the phenomena seen in leucoplakia. He also noted in these experiments many examples of metaplasia of the columnar cervical epithelium. He is of the opinion that cervical cancer is the result of a disturbed balance between hypophyseal and ovarian activity, associated with altered conditions of their final receptor, i.e. diseased cervical tissue.

Results of Operations on the Cervix Uteri with Special Reference to Strictures.

Before discussing the results of 261 operations on the cervix performed by 19 different surgeons, the author gives a short description of the methods advocated for the treatment of chronic infection and old lacerations of the cervix from the original operation of Sims to the modern methods of diathermy and conization. He lays stress upon the need of evaluating the type of operation by the amount of scar tissue formed at a later period, and says that he is doubtful whether it is less in the diathermy methods, where large areas have to granulate before healing, than in a well-performed Sturmdorf's operation. The cases which he investigated had all had some type of operative treatment instead of diathermy, and he reports his results.

Fifty-nine cases were treated by high amputation, and all of them were cured of the symptom of discharge. In 32 of these (54 per cent) some degree of stenosis of the canal was found—23 failing to allow the passage of the finest probe. These cases of stenosis were mostly post-menopausal, but six gave rise to obstruction to the flow of menstruation. Four patients became pregnant, two had premature labours, and two aborted; the previous cervical operation was blamed as the cause of these disasters in each case. Ninety-nine cases were treated by low amputation, and 87.8 per cent were cured of discharge. In 18 cases (18 per cent) stenosis of the canal was present, and in seven of these the canal was impassable to any

probe. Of the 12 patients who became pregnant four had premature labours, probably due to the previous operation.

Sturmdorf's operation was performed on 53 cases: 92.6 per cent were cured of discharge, and in only one case (1.8 per cent) was there any suggestion of stenosis. Pregnancy occurred in 10 cases, and in only one was any difficulty encountered at the labour; the dystocia was accounted for by weak pains, but it was possible that the cervix might have been the cause.

The conclusion reached by the author is that Sturmdorf's operation is practically ideal, and that he does not believe these results can be improved by diathermy.

VARIATIONS OF SERUM CALCIUM AND PHOSPHORUS DURING PREGNANCY.

The authors examined the teeth of 358 patients as early in pregnancy as was possible and continued until delivery; 215 of these also came up for a final post-partum examination. Estimations of serum calcium and phosphorus were also made, and oral cultures were taken for proof of the presence of increased numbers of *B. acidophilus*. The conclusions they reached were that there was no appreciable change in the teeth of women during pregnancy or lactation other than that which would probably occur in a similar group of non-pregnant women during the same period of time. They also found that the levels of calcium and inorganic phosphorus of the serum bore no direct relation to the condition of the teeth and that there was no rise in the average number of missing and carious teeth with the number of pregnancies experienced. They found, however, that age definitely increased this number.

RELATION BETWEEN THE EARLY AND LATE TOXAEMIAS OF PREGNANCY.

Missett investigated 127 primigravidae and 145 multiparae in order to study this relation. He found that the incidence of toxaemia in early pregnancy was about 60 per cent in both groups, and that the likelihood of a late toxaemia was in direct proportion to the severity of the early manifestations. Of the cases of moderately severe vomiting in the first three months, 57 per cent in both groups showed signs of late toxaemia, but the six cases with *hyperemesis gravidarum* were free from toxic signs and symptoms in the last three months.

PLACENTA PRAEVIA.

One hundred and two cases of placenta praevia, collected from January 1925, to September 1933, were investigated by Wilson. This series contained 68 of the incomplete and 34 of the complete types; marginal cases were not included. Conservative methods were used in 70 cases with two maternal deaths and 28 viable stillbirths. Of these methods it was found that version or the insertion of a bag gave the highest foetal mortality, but when version was performed after the bag had come away the mortality was lessened. Caesarean section was performed in 32 cases with no maternal deaths or stillbirths. The classical method was used in each case, and the author gives as his opinion that the incision should not be made through the friable pathological area.

THE IMPORTANCE OF PROPER NOMENCLATURE IN PUERPERAL SEPSIS.

The authors investigated the case-reports of over 500 cases of puerperal sepsis following full-time delivery in order to form an adequately precise and concise terminology. Among possible aetiological factors they found a high incidence during the winter and spring months, which might mean a lowering of resistance at that time or a relation to the high incidence of respiratory infections, serving as an exogenous source of infection. Prenatal care also had a profound effect on the morbidity rate, as is generally acknowledged. While analysing the labours they found that early rupture of the membranes and long labours were not predisposing factors in the production of sepsis. An almost equal number of deliveries occurred spontaneously at home and at the hospital; yet the mortality of infection at home was four-fold as compared to that in the hospital. A practically similar difference was found in the percentage of septic cases in the operative deliveries when delivered at home or in hospital. Thirty-five per cent of the cases had been subjected to operative and intra-uterine manipulations—a high figure when compared to the usual operative incidence of six per cent. The authors found in their first series of over 400 cases that the clinical pathological diagnoses were incomplete, but that in a subsequent series of 100 cases these were improved, and details of bacteriological investigation were added. Their opinion is that therapy in puerperal sepsis becomes rational if the various types of infection are classified, and that the much abused serum therapy could be properly applied if the diagnosis is made early as to the causative oragnism and stage of progress of the pathological changes. They, therefore, plead for an aetiological and anatomicopathological terminology, including the type of organisms responsible, in order to obtain more accurate mortality statistics, more accurate prognosis, and more rational therapy.

THE CONSTITUTIONAL ORIGIN OF CEREBRAL DISEASE IN THE NEWBORN.

During a course of study of a group of infants suffering from various complaints the author recognized that the possibility of true tetany was a fact. He also noticed that this tetany was often associated with generalized oedema and symptoms of cerebral compression, and he gives a table listing the signs and symptoms of each of these three main groups. He is convinced that generalized oedema, oedema of the brain and tetany form a clinical syndrome.

He explains the tetany on a low ionic calcium content of the blood brought about by a low total calcium (calcium starvation or parathyroid deficiency) or by alkalosis. Alkalosis itself is caused by many abnormal conditions, such as excessive vomiting, but he contends that in the newborn the commonest cause is an anoxaemia induced by irregular and inefficient respirations which act as a determining factor in an infant otherwise predisposed to tetany. For treatment he advises the administration of extra calcium to the expectant mother and the early institution of active treatment in the infant. The anoxaemia can be relieved by the inhalation of carbon dioxide mixed with oxygen.

COPPER IONIZATION FOR THE TREATMENT OF LEUCORRHOEA IN VIRGINS.

Tovey suggests a new form of treatment for the intractable discharge seen in some virgins. He has found the causal organism to be the gonococcus, the streptococcus, or the colon bacillus; and often the infection is mixed. Whatever is the cause he maintains that the usual treatment of the vulvo-vaginitis with douches is totally inadequate as the focus of infection is situated in the cervix. He describes his technique of copper ionization with the use of his special small-sized copper intracervical electrode. In one case, a pinhole os with erosion, he set free half a dram of foul smelling pus after the application of the electrode to the external os. He advises four to eight applications of 20 minutes' duration each with a current of from four to 10 milliamperes given with the positive pole.

A VAGINAL STETHOSCOPE FOR USE IN LOCATING A PLACENTA IN THE LOWER UTERINE SEGMENT.

Turman discusses the maternal and foetal death-rate in placenta praevia and stresses the importance of a method of early diagnosis which does not preclude the chance of an elective method of treatment. He points out that, at present, the only recognized method is to feel the placenta through the dilated cervix, but that often this is uncertain, and in many cases the cervix is completely closed. Therefore he advocates the use of his vaginal stethoscope, whereby he is able to diagnose the abnormal position of the placenta by auscultation through the vaginal fornices. He reports that he is able to differentiate the sound of the placental bruit from that heard in the venous sinuses of the broad ligaments or uterus, and that thus far the stethoscope has yielded accurate findings in all cases in which it has been employed.

UROLOGICAL COMPLICATIONS FOLLOWING PELVIC IRRADIATION.

As the radium treatment of cancerous and non-cancerous lesions of the female pelvic organs is so popular and necessary, Everett's paper on the complications of irradiation affecting the urinary system is full of interest. He first describes a case in which bilateral infected hydronephrosis resulted from the contraction of scar tissue in the parametrium causing stenosis of the intrapelvic portion of the ureters. This followed radium and deep X-ray therapy for carcinoma of the cervix. At operation the broad ligament portions of both ureters were found to be embedded in dense scar tissue producing almost complete obstruction; both ureters were enormously dilated and a fistulous communication was present between one ureter and the peritoneal cavity. He also investigated 18 cases with urinary complications following pelvic irradiation and gives a brief description of the records of eight of them. Of these 18 cases seven had vesico-vaginal fistula, and of these seven all but one had proved ureteral stricture. The other 11 patients all had bilateral ureteral strictures, most of which were extremely dense. The author points out that in this series most of the cases of carcinoma were very advanced, and yet were free of the disease after treatment with radium, proving the efficiency of this method of treatment. In two cases, however, the carcinoma was extremely early, and he looks upon the development of fistula as being an instance of an unfortunate event. He maintains

that when radium is properly administered the incidence of fistula formation is not more than two per cent. In three of the cases the irradiation was done for benign myoma, in each case the symptoms were not relieved, and in two of them hysterectomy was performed later. He feels that radium should not be advocated in the treatment of such conditions, as the mortality for hysterectomy in cases in which there is no contra-indication for the use of radium is only about one per cent.

THE VALUE OF HORMONAL STUDY IN THE DIAGNOSIS OF CHORION-EPITHELIOMA.

Again we have an article setting forth the importance of controlling the follow-up of a case of vesicular mole with the Aschheim-Zondek and Friedman tests. Kimbrough describes the variations in the test from Neumann's two cases which were negative from three weeks after instrumental evacuation to another author's case which was positive six months after a spontaneous evacuation and was only negative following curetting. He gives as his opinion that the presence of prolan in the urine in increasing concentration longer than two weeks after the termination of a normal pregnancy, whether premature or at term, or longer than two months following the expulsion of a hydatidiform mole, is strongly indicative of chorion-epithelioma —likewise the reappearance of a positive reaction following one or two negative ones. He reports a case in which the diagnosis of chorion-epithelioma was made by a persistently positive Friedman's reaction following the expulsion of a mole, and especially by a strong reaction with one cubic centimetre of urine on the thirty-second day. The patient also developed bilateral cystic ovaries during the second week with an enlargement of the uterus; the diagnosis was confirmed at operation without a previous curettage.

CANCER OF THE CERVICAL STUMP FOLLOWING SUB-TOTAL HYSTERECTOMY.

By studying a number of cases of stump carcinoma following sub-total hysterectomy Von Graff adds another contribution in favour of total hysterectomy in all cases in which the uterus has to be removed. He first stresses the point that the cervix is endangered by malignancy far more than any other part of the female genitalia, 57.4 per cent of the total number of malignant tumours being found in this location. Twenty-two cases in which carcinoma had developed in the cervical stump represented 8.3 per cent of 263 cases of carcinoma of the cervix, and this fact alone proves that if the cervix had been removed with the uterus there would have been a considerable decrease in the incidence of cancer of the cervix. After investigating the relative frequency of stump carcinoma in the contributions of various authors from 1907, he found the figure was 0.62 per cent. He owns that this figure would not justify the giving up of the sub-total operation in favour of the total unless the danger of both operations was the same always, and not only in the hands of experts; but when the problem is looked at from the other side the picture changes, as more than four per cent of the cervical cancers of these authors developed in patients on whom sub-total hysterectomy had been performed.

Of 581 cases of stump carcnioma, 137 cases (23.5 per cent) developed the malignant change within 12 months; i.e. it is almost certain that the carcinoma was present at the time of the original operation. Four hundred and

forty-four cases (76.5 per cent) developed the disease later, so all these cases would have been saved by total hysterectomy. He maintains that as considerably more than half of the patients with stump cancer die these losses should be added when the low mortality of the sub-total operation is calculated. It is generally the practice to perform the sub-total operation when the patient has never been pregnant, but Von Graff points out that in 300 cases of stump cancer in which the records were complete, 22 per cent had never been pregnant. In discussing the advisability of performing the operation of coring out the canal as being simpler than total hysterectomy, the author asserts that more than 80 per cent of all cancers of the cervix develop from the squamous cells of the vaginal surface.

EFFECTS OF CHLORAL HYDRATE ON THE MATERNAL AND FOETAL ORGANISMS.

Chloral hydrate is chemically closely allied to chloroform, and as the latter drug is known to have a deleterious effect on the liver and kidneys during pregnancy, the author instigated a series of experiments on pregnant dogs to investigate the effect of chloral. His experiments involved the administration of chloral hydrate and the study of the liver and kidneys of the dogs and their pups *in utero*, both before and after the administration of chloral. Eighteen dogs were used in this study, and in each case decidedly degenerative changes were found in the liver and kidneys of the dogs and their pups. The author thus comes to the conclusion that this drug has a definite and serious action on the liver and kidneys and is certainly contra-indicated in all cases of toxaemia of pregnancy and eclampsia—this view is directly opposed to Stroganoff's treatment of eclampsia.

MALIGNANCY IN CERVICAL POLYPI.

Fetterman points out that all cervical polypi are exposed to trauma and inflammation, and that during the process of healing the original simple columnar epithelial covering is replaced by a squamous epithelium which tends to undisciplined growth. Malignant degeneration in polypi is rare, and many cases have been diagnosed as malignant unnecessarily. The author reviews the pathological reports of 100 polypi of which six were reported as malignant. The malignant change was that of squamous carcinoma. Three of these occurred in a uterus already the site of cancer (two of body, one of cervix) while the remainder were removed for the cervical lesion alone. The author came to the conclusion that all polypi should be thoroughly examined and that close co-operation should take place between the surgeon and the pathologist if malignancy is suspected.

AN ENDOMETRIAL THEORY OF ECTOPIC PREGNANCY AND AN INTRALIGAMENTOUS PREGNANCY AT SIX MONTHS.

Schenck and Frankel report a case of intraligamentous pregnancy with the removal of a living six-months' child. They also bring forward a theory that all abdominal pregnancies, and many cases of tubal pregnancy, occur because of the presence of aberrant endometrial tissue undergoing decidual change and attracting the fertilized ovum to embed in its abnormal situation.

B. Jeafferson.

The Journal of the American Medical Association

Vol. ciii, No. 9, September 1st, 1934.

*Chorion-epithelioma: early diagnosis by the quantitative determination of anterior pituitary-like principle from the urine of pregnancy. M. L. Leventhal and W. Saphir.

The Dionne quintuplets. A. R. Dafoe. (Current Comments.)

Vol. ciii, No. 10, September 8th, 1934.

*Breast and artificial feeding: influence on morbidity and mortality of 20,000 infants. C. G. Grulee, H. N. Sanford, and P. H. Herron.

Contraception and birth control. (Editorial.)

Vol ciii, No. 11, September 15th, 1934.

*Carcinoma of the uterine cervix. H. Schmitz and E. L. Benjamin.

Vol. ciii, No. 15, October 13th, 1934.

*Reduction of premature infantile mortality through determination of foetal size in utero: an attempt to control weight at birth according to the complication of pregnancy present.

Phase of sterility. C. H. Birnberg.

Vol. ciii, No. 16, October 20th, 1934.

The Krukenberg tumour: report of a case with rectal involvement producing stricture. F. G. Runyeon.

*Value of Friedman's test in the diagnosis of intra-uterine and extra-uterine pregnancy. M. A. Goldberg, U. J. Salmon, and R. T. Frank.

CHORION-EPITHELIOMA: EARLY DIAGNOSIS BY THE QUANTITATIVE DETERMINATION OF ANTERIOR PITUITARY-LIKE PRINCIPLE FROM THE URINE OF PREGNANCY.

The authors describe a case of chorion-epithelioma of the uterus which is entirely confined to the myometrium and which was diagnosed by the Zondek-Aschheim test and subsequently treated by pan-hysterectomy. The Zondek-Aschheim test was negative with undiluted urine 43 days after operation.

A method for the quantitative estimation of anterior pituitary-like substance in the urine is described, using infantile mice and employing urine diluted in varying proportion with normal physiological saline solution.

It is pointed out that the quantitative determination of the gonadotropic substance in the urine is an important biological test in the early diagnosis of chorion-epithelioma and, in the absence of clinical manifestations, an amount of gonadotropic substance in the urine in excess of 20,000 mouse-units per litre indicates the formation of an early chorion-epithelioma. Recurrence of chorion-epithelioma or metastases may be discovered by the Zondek-Aschheim test and this should determine the use of radio-therapy.

BREAST AND ARTIFICIAL FEEDING: INFLUENCE ON MORBIDITY AND MORTALITY OF 20,000 INFANTS.

In a study covering 26,061 infants from birth to nine months during the years 1924 to 1929 inclusive, 48.5 per cent were totally breast-fed, 43.0 per cent were partially breast-fed, and 8.5 per cent were artificially fed. The

total morbidity of the breast-fed group was 37.4 per cent, of the partially breast-fed group 53.8 per cent, and of the artificially-fed group 63.6 per cent.

The average mortality of these infants per year was 1.1 per cent. Of this mortality 6.7 per cent were in the breast-fed group, 27.2 per cent in the partially breast-fed group, and 66.1 per cent among the artificially-fed group.

In the classification of infantile morbidity the cases were divided into three groups, i.e. respiratory, gastro-intestinal, and unclassified, and the increase in the morbidity was proportionate to the main figures in the three groups of cases.

The artificial feeding recommended in all cases was cow's milk (boiled for five minutes), one and a half ounces to the pound of body-weight with water added to make up to two and a half or three ounces of fluid per pound of body-weight, and one-tenth ounce of cane sugar to the pound body-weight was then added. The latter was restricted to not more than six teaspoonfuls in 24 hours. Accessory foods were added as follows: Orange juice, beginning with one half-teaspoonful every 24 hours at four weeks, increasing to eight teaspoonfuls at five months, and cod-liver oil, ten drops during 24 hours at six weeks, increasing to three teaspoonfuls at five months. Cereal was added at five months, vegetable at six months, and the second cereal at eight months.

Reduction of Premature Infantile Mortality through Determination of the Foetal Size in Utero.

Further reduction in the high premature infantile mortality depends on reducing the number of deaths in the first 48 hours of life. The condition of the premature infant at birth may be improved by delaying the induction of labour until an infant of adequate weight can be assured. An estimation of the weight of the infant *in utero* can be made through measurement of the occipito-frontal diameter of the foetal head by means of a modified radiological technique, which diameter may be translated into terms of expected body-weight.

In the more severe grades of toxaemia a situation may arise in which it is safer for the foetus to take its chance of being delivered as a premature infant than to run the risk of being stillborn should pregnancy be allowed to continue. The risk to the foetus of being delivered as a premature infant can be determined from information as to its expected birth-weight. In reaching a decision this is compared with the chance of foetal death *in utero* as determined by an evaluation of the severity of the toxaemia.

In pregnancy complicated by cardiac disease, without failure, there is little danger of death of the foetus *in utero*, and pregnancy may be allowed to continue as long as the maternal condition will permit. It is important that delivery should not be delayed until congestive cardiac failure develops, for, in these circumstances, the premature infantile mortality amounts to 80 per cent.

The influence of knowledge of the weight of the foetus *in utero* in the management of certain types of pregnancy is felt to have contributed to the reduction in the stillbirth-rate to 47 in 1933, from a level of 69 per 1,000

deliveries for the preceding 10 years. This evidence is based on statistics obtained from 30,781 births under the supervision of the Boston Lying-In Hospital during the last 11 years. The knowledge of the weight of the foetus *in utero* has been instrumental in increasing the incidence of premature infants born alive from an average of 27.6 for the preceding 10 years to 34.7 per 1,000 deliveries in the year 1933. The proportion of premature infants weighing from four to five pounds at birth increased from an average of 52 per cent for the preceding 10 years to 61 per cent in 1933. The premature infantile mortality also dropped from 35 per cent to 29 per cent.

VALUE OF FRIEDMAN'S TEST IN DIAGNOSIS OF INTRA-UTERINE AND EXTRA-UTERINE PREGNANCY.

The Friedman test for pregnancy is a valuable laboratory aid in the diagnosis of this condition, but it has its limitations. For the clinician it is important to remember that a positive test means merely that the patient is excreting anterior pituitary-like hormone which is formed in response to the presence of viable chorion, that the positive test does not indicate whether the foetus is alive or dead, that the test will remain positive in missed and in incomplete abortions as long as viable chorion is attached to the uterine wall, and that a negative test does not exclude the presence of an ectopic gestation.

In 1,093 normal intra-uterine pregnancies the percentage of falsely positive Friedman's tests was 0.09. The percentage of false negatives was 0.55 This small percentage of error, as compared with other reports, is attributed to the fact that duplicate tests were performed. At least 3.4 per cent of rabbits appear to be refractory to the Friedman test.

In ectopic pregnancy, the percentage of false negatives in a series of 44 cases was 32. This high percentage of false negatives is attributed to the presence of dead or degenerated villi in these cases, for in both intra-uterine and extra-uterine pregnancy the Friedman test is dependent on the viability of the chorion.

In missed abortion the Friedman test may remain positive for as long as 30 days after the death of the foetus. In incomplete abortion the Friedman test may be positive. The presence of a viable foetus can be determined by study of the female sex hormone of the blood.

In the diagnosis of ectopic pregnancy, the Friedman test is only of value when it is positive, and if it is negative in a case of suspected ectopic pregnancy, the clinical history and observations should determine the diagnosis.

John Beattie.

Surgery, Gynecology and Obstetrics.

Vol. lix, No. 4, October 1934.

*Malignant disease of the female generative organs in the first three decades of life. B. F. Schreiner and W. H. Wehr.

*Dial-urethrane for obstetrical analgesia. Porter Brown.

*Benign structure of the intestine due to irradiation of carcinoma of the cervix uteri. E. N. Collins and T. E. Jones.
*Torsion of the fibromatous uterus; a surgical emergency. M. A. McIver.
*The toxaemias of pregnancy. W. J. Dieckmann.

Vol. lix, No. 5, November 1934.

*The lipoid composition of white blood-cells in women during pregnancy, lactation, and the puerperium. E. M. Boyd.

MALIGNANT DISEASE OF THE FEMALE GENERATIVE ORGANS IN THE FIRST THREE DECADES OF LIFE.

There were 2,405 patients admitted to the State Institute for the Study of Malignant Disease, Buffalo, up to October 15th, 1933. On going through the records the authors were surprised to find that 114, or 4.6 per cent of these patients, were 30 years of age or younger.

The most common malignant gynaecological disease in this group of patients was epithelioma of the cervix, which was found in 68 per cent of the cases. Ovarian malignancy occurred in 23 patients, but malignant disease of the fundus of the uterus, of the vagina and vulva, was less frequent.

Cervical cancer in groups I and II has had a cure-rate similar to the general average cure-rate in cancer of the cervix, namely 50 per cent and 33 per cent respectively. Groups III, IV and V have been only palliative.

One case of epithelioma of the vagina which occurred in a patient four months pregnant and which was treated by irradiation is reported. A normal healthy child was born, and up to 14 months recurrence had not been reported.

This statistical paper was written with the sole purpose of calling attention to the frequency of malignant disease of the female generative organs at the early age of 30 years or less. The only hope of discovering and treating early lesions of the cervix lies in careful gynaecological examination bimanually and with a speculum, resorting to biopsy and cauterization in the so-called cervicitis and erosion to rule out or discover malignancy.

DIAL-URETHRANE FOR OBSTETRICAL ANALGESIA.

The author has used dial-urethrane solution in 56 patients, and he is convinced that if used according to his method, it is the most satisfactory obstetric analgesic ever employed.

His technique is as follows: The patient is told that she will feel relaxed and sleepy from the injection, otherwise alarm may be experienced over the peculiar sensation. Four cubic centimetres of the solution are drawn into a syringe of the capacity of five cubic centimetres and the needle thrust through the wall of the vein. Injection is made slowly, the patient being constantly questioned and the injection discontinued when she no longer responds. In some cases, two cubic centimetres will suffice, in others the full four may be necessary, but the author has never given more than four cubic centimetres. If sound sleep does not occur between pains, a second injection

of two cubic centimetres is given in 30 minutes. Further injections each of two cubic centimetres may be given, but the author has not exceeded a total of eight cubic centimetres in the course of any labour.

There were no stillbirths in this series, nor were there any instances of serious respiratory depression in the child.

Far-reaching conclusions can scarcely be drawn as to the safety of dial-urethrane, because there was only a limited number of cases in this series, but the author notes that Nelson, in a series of 110 cases, records no undesirable sequelae, and Massey, in a series as large and with a dosage 50 per cent greater, concludes that the preparation is perfectly safe.

Benign Stricture of the Intestine Due to Irradiation of Carcinoma of the Cervix.

In a series of 422 patients with cervical carcinoma who have received irradiation therapy at the Cleveland Clinic there have been six cases of benign stricture of the intestine, which might easily have been confused with metastatic carcinoma. The present study directs attention to this benign lesion as a clinical entity, and offers suggestions for its prevention, the results of which will be reported in a later communication.

If an irradiation stricture develops in a localized segment of intestine because this segment, during the time of the radium irradiation, remains constantly in one position, adjacent to the area being treated, the lesion should be prevented if the position of this segment can be changed at intervals during the time the radium is in place. This complication may well be prevented without altering the principles of the well-proved present-day efficacious irradiation therapy of cervical cancer, and when treated so successfully by surgical intervention, it should not constitute a retarding influence on such therapy.

Torsion of the Fibromatous Uterus; a Surgical Emergency.

A case is reported of a fibromatous uterus occurring in a woman 62 years of age and producing acute symptoms and collapse. Pre-operative treatment consisted of transfusion of blood and intravenous glucose infusions; operation was supra-vaginal hysterectomy under local anaesthesia, and the patient recovered.

Approximately 140 cases have been reported in the literature, eight being from the United States. These latter cases are abstracted together with six cases from other countries.

In considering the pathology the authors noted that the tumour responsible for the twist is usually large, and may be single or multiple, sessile or pedunculated. The torsion usually takes place at the isthmus; the twist is commonly from left to right and may be through as few as 90 degrees or as many as 450.

There are a number of factors regarding the aetiology which are not clear, but the authors have noted certain facts. There is usually a thinning and stretching of the isthmus as the tumour increases in size, so that this structure forms a pedicle which may readily be twisted. Asymmetry in the growth of the tumour may be a factor In the torsion.

The cases fall into two clinical groups; one giving an acute, fulminating picture similar to that encountered in twisted ovarian cysts or pedunculated fibroids, and the second presenting mild symptoms continuing over a number of years.

Prompt operative treatment is indicated with appropriate pre-operative treatment to combat shock, if this complication is present.

THE TOXAEMIAS OF PREGNANCY.

During the past nine years the author has been interested in toxaemias of pregnancy and has been making various investigations; he has had unusual opportunities of examining, studying and treating 700 toxaemic patients, of whom 75 had eclampsia. Examination was made in 3,688 samples of blood and 2,000 specimens of urine.

In one table the author summarizes the number of severe and moderately severe toxaemic patients admitted to the Chicago Lying-In Haspital, over a period of two years and seven months. Out of 438 toxaemic patients there were only nine maternal deaths, four only being immediate and the other five after six months. The low maternal mortality is due to an early termination of pregnancy either by the induction of labour or Caesarean section if near term, or by abdominal hysterectomy if discovered early in pregnancy. In the second table the data for the eclamptic patients is summarized. One maternal death occurred in a total of 30 patients.

The general rule carried out at Chicago with these patients is as follows: If the pregnancy is less than 28 weeks, and if after a period of seven to 10 days of observation, study and treatment, the symptoms and signs become worse, the pregnancy is terminated. If the patient is seen after the twenty-eighth week of gestation, and if after seven to 10 days of observation and treatment there is no improvement, the pregnancy is terminated. But, if there is any amelioration of the signs and symptoms with rest in bed, diet, elimination and sedatives, interference is not indicated.

The author believes that there will always be toxaemias of pregnancy, but proper rest, elimination and diet will reduce their incidence.

THE LIPOID COMPOSITION OF WHITE BLOOD-CELLS IN WOMEN DURING PREGNANCY, LACTATION, AND THE PUERPERIUM.

The lipoid content and distribution in white blood-cells of 11 women at or near the termination of pregnancy, during lactation and the puerperium, has been studied under controlled conditions of diet and exercise. It was found that age and parity did not affect the amount of lipoids in the leucocytes.

Before parturition the white blood-cells have a wide range of lipoid values, though on the average, cholesterol ester and neutral fat are low in amount and the total lipoid content is reduced by about one quarter from the mean levels in non-pregnant women.

Following parturition there is no change in the lipoid composition of the blood leucocytes until the third to the seventh day. Then a rise in total lipoid occurs, due to increases in phospholipoid, free cholestrol and neutral fat. These high values appear to return to normal, the return beginning about three weeks after delivery. Cholesterol ester is present in small amounts throughout.

On the basis of current theory these results have been interpreted as indicating an increased activity on the part of the white blood-cells during the first two to three weeks of the puerperium. The causes of this phenomenon have been discussed in this paper and a short review of the phyisological chemistry of the blood leucocytes included.

C. D. Read.

The American Journal of Cancer.

Vol. xx, No. 1, January 1934.

*On some effects produced by applying oestrin to the skin of mice. H. Burrows and N. M. Kennaway. (From the Research Institute, Cancer Hospital, London).

Vol. xxi, No. 3, July 1934.

Adenocarcinoma of the uterus in a rabbit. Oran I. Cutler.

Vol. xxi, No. 4, August 1934.

Tumours of the breast related to the oestrin hormone. Charles F. Geschickter, Dean Lewis and Carl G. Hartman.

Vol. xxii, No. 1, September 1934.

*The incidence of vaginal fistulae in patients with carcinoma of the cervix. Frank R. Smith.

On Some Effects Produced by Applying Oestrin to the Skin of Mice.

In these experiments mice of both sexes were painted daily with oestrin, applied to the non-epilated skin of the back. The oestrin appears to be absorbed through the intact skin; definite changes were found in the genital organs of both sexes. In the females, there was an accumulation of keratinized epithelium in the vagina, sufficient to distend the passage and apparently to obstruct the outlet from the uterus, with consequent enlargement of the uterine horns, which were palpable during life. In addition to obstructing the uterus, the vaginal accumulations prevented a free outflow of the urine, leading to retention of urine and even hydronephrosis. In the males the following lesions were observed: scrotal herniae, atrophy of the testicles and enlargement of the posterior lobe of the prostate, the latter changes giving rise to urinary obstruction. The significance of the changes in relation to the development of carcinoma is discussed.

The Incidence of Vaginal Fistulae in Patients with Carcinoma of the Cervix.

This is a statistical paper from which the following conclusions are drawn: (*a*) That vaginal fistulae are primarily a manifestation of the advancement of the disease, the incidence being twice as high in untreated as in irradiated cases. (*b*) In patients treated by radiation, the incidence is increased by the following factors: Interstitial radon irradiation, lack of filtration, repeated treatments, infection, structural type of lesion, hysterectomy before irradiation. (*c*) The order of frequency of occurrence is recto-vaginal 1:75; vesico-vaginal 1:92; a combination of both recto-vaginal and vesico-vaginal fistulae 1:129.

A. C. Bell.

American Journal of Diseases of Children

Vol. xlvii, No. 2, February 1934.

*The blood during the first year of life: (II) the anaemia of prematurity. Katharine K. Merritt and Leonard T. Davidson.

*Mineral growth of the human foetus. Vivian Iob and William W. Swanson.

Pneumocoruic meningitis in the newly-born: a case in an infant aged two days. Bohn F. Coppolino and Peter Gannone.

Vol. xlvii, No. 3, March 1934.

*Agglutinins in mother's blood, baby's blood, mother's milk and placental blood. John A. Toomey.

*A comparison of the Schiek and the Dick tests in mothers and in newborn infants. Alma Rothholz and Ann G. Kuttner.

Vol. xlvii, No. 5, May 1934.

*Blood-cells in healthy young infants: the leukocytic picture during the first three months. Alfred H. Washburn.

Vol. xlvii, No. 6, June 1934.

So-called breast milk intoxication. Toshiwo Tanaka.

THE BLOOD DURING THE FIRST YEAR OF LIFE: (II) THE ANAEMIA OF PREMATURITY.

In a previous paper the authors dealt exhaustively with normal values for the formed elements of the blood in the first year of life and their relation to neo-natal bleeding and the coagulation time. The present paper reviews the literature of the haematology of premature infants in regard to the formed elements, the coagulation and bleeding time, the iron-metabolism of premature infants, and the treatment of the anaemia of prematurity. They go on to report the results personally obtained in investigating erythrocytes, haemoblobin, reticulocytes, bleeding and coagulation times. They contend that by the early administration of liver and iron the anaemia of premature infants can be ameliorated.

MINERAL GROWTH OF THE HUMAN FOETUS.

Sixteen foetûs, ranging from the third lunar month up to term, were subjected to analysis by microchemical methods. Attention was paid to the nitrogen content and that of the following minerals: sodium, potassium, calcium, magnesium, and phosphorus. The values for the calcium, phosphorus, and magnesium—minerals found in the foetal skeleton—showed a gradual increase, while those for the potassium and sodium—found in the intracellular fluid and plasma—showed fluctuations. The greatest alterations in mineral content appeared to take place in the fourth lunar month.

AGGLUTININS IN MOTHER'S BLOOD, BABY'S BLOOD, MOTHER'S MILK, AND PLACENTAL BLOOD.

The literature of investigations of the agglutinin-content of the mother's serum and that of her newborn offspring, both in man and in animals, is discussed. The high agglutinin-content of milk, particularly colostrum, has

been advanced as the explanation for the appearance of these bodies in the serum of the newborn after birth. In the present investigation agglutinins against the enteric group of organisms were found in the placental blood, thus showing that in the human infant transmission through the placenta occurs. The degree of this transmission was comparatively slight as judged by a comparison of the titres of placental blood-serum and mother's blood-serum. The blood of the infant 10 days after birth contained a much higher titre and in a general way paralleled the titre of the mother's milk. The early milk contained more agglutinins than did later specimens; in no instance was the titre greater than that of the mother's serum. By deduction it appears that agglutinins reach the foetus in the first place by placental transmission, and in the second by absorption of ingested agglutinins; but auto-production cannot be ruled out. During this investigation a mixture of 21 strains of enteric organisms were employed.

A Comparison of the Schick and the Dick Tests in Mothers and Newborn Infants.

In accordance with the observations of previous workers, the Schick and Dick tests have been found unreliable in new-born infants. No adequate explanation has been found for the discrepancies observed between the reactions of adults and newborn infants with either of these tests. It seems possible that the failure of newborn infants to react to them in the absence of antitoxin may be related to a non-specific property of the skin of the newborn, which is known to be refractory to substances of primary toxicity such as eel's serum and chemical irritants. (Authors' summary.)

Blood-cells in Healthy Young Infants: The Leucocyte Picture during the First Three Months with Special Reference to Hourly and Daily Variations.

Accurate information concerning the possible variations in the leucocyte count of a healthy infant are not to be found in modern paediatric textbooks, and the presentation of average figures does not indicate the magnitude of normal variations.

The hourly fluctuations were studied in six healthy infants during the first 16 weeks. Irregular fluctuations of the total leucocytes were noted in the same baby at the same hour of different days, and for different babies of the same age and size at the same hour. For any one baby the smallest variation was from 5,900 to 13,300, and the greatest from 8,800 to 23,150 (i.e. minimal variation 116 per cent, maximal variation 200 per cent). The curves for the lymphocytes tended to parallel these for the total leucocytes. The author concluded, *inter alia*, that the leucocytic count may be expected to vary from 4,000 to 23,000 per cubic millimetre without indicating the presence of demonstrable disease. There was no orderly rhythm in the changes he noted, and no apparent correlation with factors such as digestion, sleep or increased activity. Lymphocytic vaiations were mainly responsible for the great fluctuations observed.

Reginald Lightwood.

La Gynécologie.

August 1934.

*The forceps. L. Demetin.
Proceedings of the Society of Obstetrics and Gynaecology of Vienna.

September 1934.

*The forceps. L. Demetin.

THE FORCEPS.

Both the August and September numbers of this periodical are devoted to an account of the forceps by Demetin. He gives a comprehensive survey of the subject from the historical, theoretical, and clinical aspects. Most of the best known varieties of the instrument are discussed, and the author has spent much time, thought, and experiment on the subject and has devised several types of his own. He thinks that there is still room for research.

The shanks of his own forceps do not cross as, mechanically, he considers the ordinary crossed shanks unsound in theory. The uncrossed shanks are claimed to give a greater area of application to the skull and also the movement between forceps and skull is lessened. Thus traction is improved.

In axis traction he believes that the more usual methods can be improved and in order to apply the tractive force at the best point (the bi-auricular diameter) the blades of the author's forceps have foramina in them placed nearer to the free end than in Milne Murray's or Tariner's forceps. There are two foramina to each blade, superior and inferior, and the tractors are not rigid rods but composed of a double length of firm tape threaded through the foramina. As either set of these latter can be used, it is possible to flex the head as much as possible in all positions, and the tapes give a universal joint. The tapes are stored, sterilized, in glass containers, and will stand a tensile strength of 100 kilogrammes.

R. K. Bowes.

Gynécologie et Obstétrique.

Vol. xxix, No. 6, June 1934.

Memoir of the late Professor Adolphe Pinard.
*Malignant tumours of the ovary in pregnancy. Trillat and Puthod.
*The value of intravenous pyelography in the diagnosis of urogenital fistulae. Dobrzaniecki and Grabowski.
A case of mesenteric thrombosis in the eight month of pregnancy.
The Bordet-Gengou reaction in gynaecology.

Vol. xxx, No. 2, August 1934.

*The control of labour. Voron and Pigeaud.
The toxic factor in placenta praevia. Nubiola.
Blood-transfusion and its use in gynaecology. Serdukoff and Leviskaia.
Bacillus coli infections in gynaecology. Guillemin.
Haematoma of the rectus abdominis muscle during pregnancy. Brindeau.

No. 3, September 1934.

Cases of spontaneous thrombo-phlebitis associated with uterine fibroids. Cotte and Mathieu.

Puerperal thrombo-phlebitis causing subacute septicaemia. Ducuing and Guilhem.

°The anaemias of the foetus. Pehu, Trillat and Noêl.

*Diffuse oedema of the foetus with a note on the histological appearances. Kulikowska.

*A contribution to the radium therapy of carcinoma corporis uteri. Held.

Two cases of foetal abnormalities. Agaronian.

MALIGNANT TUMOURS OF THE OVARY IN PREGNANCY.

Two cases of malignant ovarian tumours, the one a lympho-sarcoma, the other a papillary carcinoma, associated with pregnancy are reported. The authors stress the absence of symptoms in such cases until the onset of dystocia calls attention to their presence. In one of the cases the tumour was shown to have been present before conception occurred. Discussing the effect of malignant ovarian tumours on the development of the foetus, the authors conclude that pregnancy usually proceeds normally. Evidence of either an adverse or a beneficial effect of pregnancy upon the growth of the tumour is still inconclusive.

THE VALUE OF INTRAVENOUS PYELOGRAPHY IN THE DIAGNOSIS OF UROGENITAL FISTULAE.

The authors have examined a series of puerperal urogenital fistulae by means of intravenous pyelography. In most of the cases the primary lesion was a widespread necrosis around the vaginal vault and the resultant scar tissue had produced much distortion of the bladder, the lower parts of the ureters and the vagina. Filiform fistulae as a result were more commonly found associated with back pressure phenomena than with the larger fistulae where the bladder had prolapsed into the vagina. Intravenous pyleography is the only satisfactory method of determining the degree of ureteral compression in such cases.

THE CONTROL OF LABOUR.

The authors discuss the efficacy of the available methods of expediting normal labour. They have found artificial rupture of the membranes accelerate delivery, provided that labour has definitely started and the diameter of the os has reached three to four centimetres. The membranes are regarded merely as a protection against ascending infection, their dilating effect being reckoned as negligible. The only other method they have found of constant service has been the use of pituitrin in cases of inertia. They have found that a dose not exceeding two international units overcomes inertia in both the first and second stages and is not attended by ill effects.

THE ANAEMIAS OF THE FOETUS.

The authors discuss the morphology of the foetal erythrocytes, the development of which they describe in three phases. In the first phase,

occupying the first few weeks of foetal life, the erythrocytes develop in the blood islands, forming first nucelated primitive erythroblasts, which then lose their nuclei to form primitive megalocytes. In the second phase, lasting from the third month until term, the erythrocytes develop in the liver and spleen. The cells are first basophile, then polychromatophile, finally acidophile, after which the normoblast loses its nucleus to become a normal blood-corpuscle or normocyte. The third phase of medullary haematogenesis commences just before term.

Certain disorders of the foetus and the newborn are attributable to foetal blood dyscrasias. These are, generalized oedema of the foetus, congenital familial jaundice, the acute anaemia of the newborn and the acute congenital leukemias.

The authors describe a case of generalized oedema in a foetus born macerated at the fifth month. The only abnormality found on histological examination was a pronounced excess of blood islets in all the organs of the body, even in tissues not normally blood-forming organs. The heart blood contained a marked excess of megaloblasts. The authors describe similar changes which they found in a newborn child which died as a result of severe familial jaundice.

DIFFUSE OEDEMA OF THE FOETUS.

The author describes the histological appearances found in a case of diffuse oedema in a syphilitic stillborn child. The most striking feature of the sections was the enormous excess of blood islets in the tissues, particularly the liver. The question whether diffuse oedema should be regarded as the result of a blood dyscrasia is discussed and a bibliography of the subject given. The author is of the opinion that syphilis is still to be regarded as the most important primary cause of diffuse oedema, but that its mode of action as an aetiological factor may be the toxic effect it exerts on the foetal blood-forming organs.

CONTRIBUTION TO THE RADIUM THERAPY OF CARCINOMA CORPORIS UTERI.

The author re-asserts the fact that, in cases of carcinoma of the body in which the cavity is enlarged or distorted, a more effective irradiation is obtained by the use of multiple intra-uterine foci than with a single tube.

P. Malpas.

Bruxelles Medical.

No. 38, July 22nd, 1934.

*Interischial pelvimetry. Max Cheval.

No. 39, July 29th, 1934.

Fibromyoma of the upper lip in a newborn child. R. Bourg.

No. 41, August 12th, 1934.

A case of fibromyxoma of the ovary. Pastiels.

No. 42, September 2nd, 1934.

A case of 15 years' temporary artificial menopause by radium, followed by pregnancy and normal labour. Jean Roffart-Marin.

No. 49, October 7th, 1934.

Some useful therapeutic measures in modern gynaecology. Rene Beckers.

INTERISCHIAL PELVIMETRY.

This paper emphasizes the numerous cases in which contracted outlet gives rise to difficulty in labour, and subsequent disablement owing to damage of the pelvic floor. The author believes that the interischial diameter should be measured as a routine in antenatal examinations.

A special caliper for this purpose is described, and the measurement is made in the lithotomy position; by this technique no allowance need be made for the soft parts when taking the measurement. The actual measurements of the author's last 100 cases are given: in cases with an interischial measurement of less than 12 centimetres, routine episiotomy is done. This operation was done in 60 per cent of the cases in this series.

A. C. Bell.

Zentralblatt für Gynäkologie.

No. 38, September 22nd, 1934.

*Multiple urethrocoeles in the female. A. Baidin.

The clinical aspect of cystitis emphysematosa. T. Antoine.

Operation upon vesico-vaginal fistula and urethrocoele. W. Stoeckel.

Vesico-vaginal fistula. G. Frommolt and A. Stamatiades.

Ureteric plastic and ureteric implantation operations. B. S. ten Berge.

Pyelitis granularis as a cause of severe bleeding from the renal pelvis. B. Ottow and J. Pahl.

Termination of pregnancy on account of pyelitis gravidarum, truly on account of pyelonephritis. F. v. Mikulicz-Radecki.

No. 39, September 29th, 1934.

*Report on the practical findings in the legal control of eugenic health and the sterilization of women with inherited disease. B. Ottow.

Operation upon ovarian cysts which cannot be completely removed. E. Melchior.

The operative method of sterilization in woman. H. Cramer.

A rare interstitial tumour in the region of Bartholin's gland. O. Wallis.

Intestinal obstruction due to a foreign body in the peritoneal cavity. A. Kummant.

The question of the clinical diagnosis of congenital defect of the diaphragm. R. Peter.

No. 40, October 6th, 1934.

*Hormonal fertilization in the hibernating bat. P. Caffier.

The pathological anatomical foundations of a raised anterior pituitary function in eclampsia and nephropathy of pregnancy. K. J. Anselmina and F. Hoffmann.

Therapeutic experiments with anterior pituitary hormone (glanduantin) in uterine cancer. L. Kriesch and K. Victorisz.

*The local homostimulant treatment of ovarian insufficiency. C. Stanca.

Preliminary report of the effect of the Coutard method on inoperable carcinoma of the ovary. A. Gegenbach.

Observations on 1,000 cases of ovarian cyst. M. Randazzo.

No. 41, October 13th, 1934.

Enumeration of labour pains and birth prognosis. F. Siegert.

The true and sensible designation of the oblique diameters of the pelvis. B. Ottow.

Resistance of the ovary to gonotropic hormones. H. Siegmund.

*In-breeding considerations in the Frisian Peninsula. K. W. Schultze.

Large stercolith simulating an ovarian cyst. G. v. Nagy.

Combined treatment by mud baths and urine excreted during pregnancy of gynaecological affections. A. Mandelstamm and S. Becker.

No. 42, October 20th, 1934.

Further results of radio-therapy of cracinoma of the uterus. F. Voltz.

Simplification of local anaesthesia for gynaecological laparotomies by the interposition of a short evipan narcosis. J. Frigyesi.

A case of decidual reaction in a cervical polypus and at the external os. J. Gosau.

Dysmenorrhoea. A. v. Fekete.

The influence of anterior pituitary hormone upon the internal genital organs of the mature woman. E. Stöcki.

Contribution to the question of cases resembling hyperemesis. P. I. Fomina.

No. 43, October 27th, 1934.

Two osteodystrophic contracted pelves, with observations upon the significance of osteodystrophia fibrosa in gynaecology. P. Esch.

Elephantiasis and pregnancy. A. Bauereisen.

Recovery from toxaemia of pregnancy especially from hyperemesis. Kj. v. Oettingen.

*Local puerperal diseases: the circulatory system. E. M. Kaplun and F. I. Witenstein.

Rare obstetric injury in breech delivery. R. Pohl.

Umbilical care in the newborn. St. Sztehlo.

No. 44, November 3rd, 1934.

The present-day limits and responsibility of tubal pregnancy. K. Fink.

*The question of internal and external migration of the human ovum. J. Gosau.

Pelvic pain. Resection of the superior hypogastric plexus for the relief of pain. F. S. Wetherall.

The vitality of autotransplanted ovaries. C. Stanca.

The importance of the bag of membranes in the dilatation of the cervix. K. Bruger.

Recurring herpes simplex (menstrualis) of the intermenstrual period with unknown localization. E. G. Abraham.

Eczema graviditatis treated successfully by extirpation of a septic focus. G. v. Bud.

No. 45, November 10th, 1934.

Results and limitations of domiciliary midwifery. P. W. Siegel.

A simple, certain, non-haemorrhagic and quickly performed tubal sterilizaton. O. Honcamp.

Fibroma ovarii adenocysticum. O. Frankl and E. Klaften.

The reaction of the uterus towards pituitrin. R. Tachezy.

Manual placental separation and the significance of pituitrin in the period after delivery. F. Bachner.

A contribution towards the clinical findings and diagnosis of tuberculosis of the adnexa. R. L. Livschina.

MULTIPLE URETHROCOELES IN THE FEMALE.

Baidin describes the case of a woman of 37 years who came for treatment on account of pain and burning on micturition which was in no way improved by vesical irrigation or medical treatment.

On local examination with the finger in the vagina three cystic swellings could be felt between it and the urethra. On cystoscopic examination no abnormality was discovered. After the injection of a diluted emulsion of barium into the urethra, X-ray investigation showed three pouches communicating with it by narrow channels.

The patient was treated by an operation to expose the urethra through an incision through the anterior vaginal wall, laying bare at the same time the three cystic swellings from which urine could be squeezed into the urethra. All three cysts were excised and their communications with the urethra closed with catgut sutures.

On microscopic examination of the excised cysts two were found to be lined with epithelium similar to that of the bladder, and the third was similarly lined in the neighbourhood of the communicating channel, but at the opposite pole the wall was similar to that of an abscess cavity.

The writer explains the condition as being the result of infection of urethral glands with temporary occlusion of their ducts and the formation of cysts. At a later stage the pressure of infected contents in the cyst is sufficient to re-open the duct into the urethra, when partial drainage of the cavity takes place, the final stage being reached when epithelialization of the cavity is brought about by extension from the gland's duct.

The writer considers that all urethral pouches in the female are acquired and not congenital.

REPORT ON THE PRACTICAL FINDINGS IN THE LEGAL CONTROL OF EUGENIC HEALTH AND THE STERILIZATION OF WOMEN WITH INHERITED DISEASE.

Ottow refers to the passing of the Law for Inherited Health which has come into being in Germany. This law has been described from the point of view of its aim and object as well as its means of fulfilment in the book known to every practitioner in Germany and written by Gütt-Rüdin-Ruttke. The practical work in connexion with the new law has come into being during the last six months, and has shown that there are many difficulties in connexion with it.

The law requires morally true co-operation of every doctor, and through him of all his assistants, such as masseurs, midwives, nurses and dentists. The medical work called for by this law falls into three groups, namely the preliminary, that of the hereditary health legal tribunal, and that of the carrying out of the sterilization. The preliminary work is the province of every medical practitioner and comprises the sifting out and classification of every case of inherited disease in the present legal sense. From this point of view it is especially the affair of the alienist, obstetrician and paediatrist. The Hereditary Health Legal Tribunal includes the following members—a State doctor, and a medical man with a special knowledge of hereditary biological lore.

The carrying out of the findings of the tribunal is not left in the hands of any doctor but sterilization is entrusted to certain hospitals only, either for men or women, or, in special cases, for both sexes. In every case the State undertakes responsibility for and supervision of the patient so treated.

The tribunal in Berlin has been divided into two sections. The writer has from the beginning been associated with the first section as Medical Assessor, and up to the present time he has helped to decide over 1,000 cases which have been brought before it. In addition the Berlin Tribunal has set aside a department in the Brandenburger Gynaecological Clinic under his care for the performance of sterilizing operations in cases in which this has been ordered by the tribunal. Up to the present time 91 cases have been legally sterilized, patients mainly being drafted here from the various psychological clinics in Mark of Brandenburg. In the course of his work in both capacities as an assessor and an operator certain problems, which need settlement, have presented themselves to him.

The patients transmitted to hospital for operation come into the practice of the operator on an entirely new footing. Ordinarily the operator has examined his patient for some personally voiced complaint, and after he has decided what the lesion is, he decides that the patient should be sterilized. Under the new conditions the patient may have no personal complaint and no gynaecological abnormality; the operator is required to abolish the continuity of the Fallopian tubes by force on an unwilling patient. In most cases the patients so treated are psychologically abnormal, and there is the added problem of the patient's reaction to any operative procedure, let alone to one to which she is actively opposed. At this point the writer emphatically points out that the law calls for every care being undertaken for the well-being of the patient who comes under the decision of the tribunal.

The tribunal, on having a case transmitted to it for judgment, has to consider whether it is one capable of transmitting inherited disease under one of the eight groups specified by the law, or whether it is a case of severe alcoholism. As most cases are sent for some mental disease, the first investigation is undertaken by a psychiatrist. The schizophrenic patient may, on account of her mental defect, be suitable for sterilization; yet because of her mental condition an operation may endanger her life from refractory behaviour after operation; in such a case operation may be contra-indicated. The patient's mental condition, therefore, is of considerable importance in deciding for or against operation; and even when operation has been decided on, it may have a great influence on the choice of operation. The con-

genitally mental defective is usually without apprehension. She is easily controlled both before and after operation; consequently she has an uneventful convalescence. Cases of congenital mental defect are, therefore, eminently suited for legal sterilization. Epilepsy is improved by the rest in bed and the administration of luminal required after operation. Other defects which may be given as reasons for compulsory sterilization will need individual consideration in the choice of operation employed.

In considering access to the Fallopian tubes, the writer points out that for some types of mental disease the abdominal incision is contra-indicated because of the danger of bursting of the wound or infection by the patient's own interference. When the patient is expected to be restless and uncontrolled she is far safer with a vaginal operation where the wound is out of reach of the patient's fingers and it is less likely to gape. In spite of the fact that in his department at the Brandenburger Clinic the patients are constantly under the supervision of nurses who have been trained in the care of mentally deficient patients, he has had one mentally defective patient who rose from bed and walked across the ward on the day following laparotomy; another patient was found with blood-covered hands, the result of access to a wound which had been carefully sutured and reinforced with adhesive plaster below the dressing.

A preliminary pelvic examination is of some importance, although it may be impossible without the administration of a general anaesthetic. Some patients, who are still *virgo intacta*, have been found to be so resistant to vaginal or even rectal examination that no information can be gained. Weak-minded women of the tramp and prostitute class are frequently heavily infected with the gonococcus, and in these it is of importance to decide whether the Fallopian tubes are involved and already occluded.

The legal minimal age for sterilization is laid down as 10 years. In actual practice the writer considers that cases are more suitably dealt with between the ages of 14 and 45 years. The choice of abdominal or vaginal route of access must depend upon the psychiatric and abdominal conditions present in each individual patient. In addition the school in which the operator has been trained and his technical skill have some bearing on his choice. In the presence of pelvic disease, such as myoma, tubal inflammation or gonorrhoea, the writer leans towards the abdominal route; but when the chief factor is a psychiatric one he prefers to operate *per vaginam*.

The writer is not willing to rely upon the existence of blocked tubes, as shown by salpingography; because the prognosis for later patency is so uncertain and often surprising. In some cases, owing to the presence of actual disease, it is found impossible to confine the operation to a simple resection of the Fallopian tubes.

It should also be remembered that a patient brought before the tribunal may already be the subject of an extra-uterine pregnancy or an intra-uterine pregnancy. The extra-uterine pregnancy obviously endangers the patient's life, and the intra-uterine nullifies the object of the new law. All operative procedures for legal sterilization must essentially consist of division of the Fallopian tubes and burying the uterine ends so that their lumina have no communication with the peritoneal cavity. The various operations for covering the ends of the Fallopian tubes are not suitable because they are

too uncertain. The writer has not himself employed Madlener's method because, in spite of the good results obtained by others, he fears that reconstruction of the tubal lumen may occur in a few cases.

The new law for legal sterilization of those who transmit inherited disease does not provide for the termination of a pregnancy which is already in existence. In the cases which have so far come under consideration there have been many who were already pregnant. In such cases it has been found that operation on the Fallopian tubes early in pregnancy has not induced abortion, and the writer has, therefore, proceeded with the instructions of the tribunal. When the pregnancy is advanced operation has been postponed until after delivery.

The writer sees no reason for any alteration in the law to allow termination of pregnancy, and considers that supervision of the offspring with later sterilization will eventually minimize the occurrence of such unwanted pregnancies. The writer is wholeheartedly in support of the new law, which he considers to be the outcome of the united will of the German nation.

Hormonal Fertilization in the Hibernating Bat.

Caffier describes the results of experiments upon hibernating female bats which were injected with anterior pituitary hormone. For his investigation the writer made use of the giant bat (*Myotis*) obtained from Dr. Eisentraut of the Zoological Institute in Berlin. He chose his animals during the early winter sleep when ovarian activity is at a standstill rather than in the spring when changes in the ovaries are beginning to appear.

It was already known that a warm temperature in itself would serve to set up ovulation. Therefore, it was obvious that this factor would have to be excluded on undertaking any investigation into the action of injected prolan. The writer obtained one male bat and five females of which the average weight was 23 grammes on January 20th, and forthwith killed one female for control. Of the remaining four femaels three were placed in the unheated attic of the laboratory, where the temperature was similar to that of their normal winter quarters, here they continued to sleep undisturbed without any food or water. The fourth animal was placed in a cage in the warm laboratory, fed and watered, eating up to 80 worms a day.

Examination of the control animal showed numerous unripe follicles in the ovaries and spermatazoa in both uterus and Fallopian tubes. Animal number 2 received the following doses of prolan, 25 rat-units on January 22nd, 50 rat-units on January 23rd, 24th, and 25th, 100 rat-units on January 26th, 27th, 29th, 30th and 31st, and 500 rat-units on February 5th. The repeated doses were given to promote ripening of the follicle, and the large dose on February 5th was given to induce the ripened follicle to rupture. This animal was killed 24 days after the last injection, and the genital organs, which had undergone no naked-eye changes, were subjected to histological examination. Serial sections of one Fallopian tube showed a mature ovum still surrounded by follicular cells and not fertilized. The corresponding ovary had a new corpus luteum which was so recent that the point of rupture was still visible. There was no other abnormfiaty in uterus, Fallopian tubes or ovary.

Animal number 3 was treated in a way identical with that in which number 2 was treated, except that it was killed on the fourteenth day after the last injection of prolan. This was done to give the ovum time to become fertilized and begin development. It was noticeable that the bat did not waken or take any nourishment throughout the experiment. Serial sections were cut in this case, and the fertilized ovum discovered in the uterus having approached a groove in the uterine mucosa but not yet being imbedded. The devolopment of the ovum had reached the morula stage. The corpus luteum was double the size of the corpus luteum in number 2, and the remaining follicles were immature.

This case showed that it was possible for an ovum to mature during hibernation as a result of the injection of prolan, and the writer supposes that the spermatozoa were sufficiently active to become motile under the influence of the liquor folliculi and to fertilize the ovum. Normally a cold temperature serves to arrest movement of the spermatozoa in hibernating animals, movement returning as the temperature of the body rises on the animal's awakening in the spring.

Animal number 4 was kept in the cold attic until it died on April 6th. While it was under observation it never awakened or took nourishment. The cause of death in this animal was not clear, but as it had survived to the season when ovarian activity normally returns, the genital organs of this animal was also subjected to serial section. Here a fertilized ovum which had developed to the two-cell stage was found in one Fallopian tube. The corpus luteum was about the same size and development as that in animal number 2.

Animal number 5 was left in the attic until April 27th, when it was killed and examined. Here a fertilized ovum was found in the uterus lying free. Its development had reached the morula stage. It would appear that ovulation begins spontaneously in *Myotis* at the beginning of April, judging from the findings in number 4 on February 6th. Hence development up to imbedding three weeks later is very slow, although growth after imbedding must be relatively rapid as the young are born between the end of May and the middle of June.

Animal number 6 was kept warm and freely fed from the beginning of the experiment. By February 14th, on abdominal palpation, a small tumour could be felt which was taken to be the pregnant uterus. One week later the animal was examined by the X-rays; the existence of pregnancy was considered to be certain, although a definite skeleton could not be demonstrated. On February 26th the animal bled from the vagina and was definitely disturbed; although no foetal parts were found it was considered to have aborted and to have eaten the products of conception. The animal was killed two days later and the post-mortem findings were consistent with such a supposition.

The Local Homostimulant Treatment of Ovarian Insuffiency.

Stanca described the case of a girl of 19 years who was epileptic and the subject of primary amenorrhoea. She had been treated with ovarian and anterior pituitary preparations and her appendix had been removed

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without any change in her condition. The writer performed laparatomy to divide the adhesions which were causing her abdominal pain. At this time he examined the pelvic organs and found them normal. Before closing the abdomen he injected one cubic centimetre of ovarian extract directly into the ovary.

Convalescence was entirely uneventful; on the twelfth day, the patient began to menstruate for the first time; the menstrual period lasted five days. Menstruation occurred for three times regularly after its first appearance and then stopped. Two years later the patient became pregnant of a male child which she carried to term. There have been no epileptic fits since her second operation.

IN-BREEDING CONSIDERATIONS IN THE FRISIAN PENINSULA.

Schultze gives a short review of the conditions under which the inhabitants of the Frisian Peninsula live. The area, practically a sandbank lying betweeen Pillau and Danzig, is isolated from neighbouring areas, and its inhabitants live by work in the woods and fisheries. The primitive and hard conditions of life on the peninsula have driven the more adventurous and strong to settle and earn their living elsewhere. The poorer stock has stayed behind, and because of its isolation intermarriage has been the rule rather than the exception. Of the whole peninsula the easternmost parish of Neukrug, with its 600 inhabitants, illustrates the changes that have resulted during the last hundred years. On examining the church register, the writer found that half the family names have died out and no names of newcomers have taken their place. Of the 65 children of school age, 20 per cent are in need of school assistance, and 54 per cent are not able to claim elementary school standing.

An investigation was made into the children of this parish in order to determine the degree of in-breeding for eight generations. They were all found to have a common ancestor eight generations back and to be very closely in-bred according to the chart drawn up by the investigator. When comparing degrees of in-breeding with bodily and mental development, as well as general physical well-being, it was found that these bore no relation to each other. In fact the children of closely-related parents appeared more fit mentally and physically than those not so closely related.

LOCAL PUERPERAL DISEASE AND THE CIRCULATORY SYSTEM.

Kaplun and Witenstein review 56 cases of illness following delivery and abortion, with the following conclusions. The function of the circulatory system suffers in nearly all cases of genital disease in which there is an accompanying noticeable functional insufficiency. In local disease with a falling temperature the heart and vascular system suffer little. A persistent rise of temperature has a definitely pathological effect. In every case in which there is uterine bleeding definite damage to the heart's action results. In considering the treatment of genital disease, it is important to devote some attention to the effect of the disease on the cardio-vascular system. Where, in addition to genital sepsis, there has been a definite loss of blood, the function of the cardiac-vascular system will be improved by blood-transfusion,

THE QUESTION OF EXTERNAL AND INTERNAL WANDERING OF THE HUMAN OVUM.

Gosau defines external wandering of the ovum as being the migration of the fertilized ovum from the ovary of one side to the Fallopian tube of the other side, through the peritoneal cavity, and internal wandering when it enters the uterine cavity by the Fallopian tube of the same side and then passes across the uterine cavity to enter the opposite Fallopian tube from within. He is at a loss to explain the mechanism of internal wandering, but supposes there must be some loss of polarity with changes in the ciliated epithelium. He records a case of internal wandering which was under his observation for 10 years. The patient had had an operation for acute appendicitis, at which time the uterus and Fallopian tubes were carefully examined. At this time the left Fallopian tube was entirely closed and measures were not taken to render it patent. Ten years later, the patient having in the meantime married and borne three children, she was operated on for a tubal pregnancy. At the operation the left Fallopian tube was found to be the site of a pregnancy which had ruptured, the abdominal end being tightly closed with old adhesions. In a second case the patient was operated on in 1929 for suspected extra-uterine pregnancy, but only a haematoma of the corpus luteum was discovered. At the time of this operation the abdominal ostium of the right Fallopian tube was found to be completely closed.

In 1933 the patient was operated on again for suspected tubal pregnancy and the pregnancy found to be present in the uterine end of the right Fallopian tube which was tightly closed at the abdominal end.

The writer is unable to explain these two cases by any other means than internal wandering of the ovum.

R. H. B. Adamson.

Münchener Medizinische Wochenschrift.

No. 38, September 21st, 1934.

*On the "menstruation poison." H. Mommsen.
*Adhesions of labia minora in children. Schlack.

No. 39, September 28th, 1934.

*Abortion. Doerfler.

No. 41, October 12th, 1934.

*The treatment of menorrhagia and dysmenorrhoea in cases of intestinal disease. R. Schwab.

No. 44, November 2nd, 1934.

*The operative treatment of non-puerperal pelvic inflammatory disease. E. Hoevelmann.

ON THE "MENSTRUATION POISON."

In former times medical men regarded menstruation as a cleansing process, nocuous substances being excreted in the menstrual blood. The laity has a similar conception of it at the present day, and also, indeed, a

number of modern medical men, including Aschner. Plants were regarded as being especially susceptible to these menstrual poisons. The owners of flower shops, breweries, etc., did not formerly employ females during their menstrual periods. The author states that the name "menotoxin" (Schick) is not good, as "toxin" suggests a definite serological entity. Lubin found that the growth of young lupines, growing in nutritive fluid, was impaired by the menstrual poison. He found this poison also in the blood, saliva and urine of menstruating subjects. Eltz states that the poison may also be found in the breast milk during lactation. Mommsen also employed the method of fermentation of glucose and yeast. The amount of carbon-dioxide developed was measured, and he found that, provided the *p*H of the solution was kept constant, menstrual blood impaired the fermentative process. The strongest action was obtained on the first day of menstruation, diminishing on each succeeding day. Occasionally the substance impairing yeast fermentation was found in the circulating blood of the subject. The author states that it is very improbable that the menstruation poison can produce ill-effects on other people, since the infant on the breast is not damaged! The nature of the menstrual poison is unknown, but it is probably derived from lipoids. Klaus thinks it is trimethylamine.

ADHESION OF LABIA MINORA IN CHILDREN.

The author reports six cases of children between two and five years of age, in whom epithelial adhesion of the labia minora occurred. The adhesion extended from the posterior commissure almost to the clitoris. Dysuria was present. Treatment consisted of separation of the adhesions with a probe. Only slight bleeding resulted. Anaesthetic ointment was employed in the after-treatment. Occasionally adhesion recurs and must be treated again in the same manner. Vulvitis is treated with a lotion of potassium permanganate and boracic ointment. This adhesion has not previously been described in the German literature.

ABORTION.

The author states that abortion is very common in Germany, and he thinks that a life is lost as a result of it every five or six minutes. He is in favour of its compulsory notification. The various types of abortion and their treatment are discussed. In incomplete abortion he advocates no vaginal packing, unless there is great danger to life from haemorrhage. Bleeding is more active in the third and fourth months, and it is better then to leave the expulsion of the foetus to nature. If interference is essential, it should be digital and not instrumental. If the cervix is not properly dilated, portions of the placenta may remain after digital curettage. Doerfler states that care in curettage must be exercised as continuation of pregnancy to full-time occasionally occurs after a supposed thorough digital curettage.

THE TREATMENT OF MENORRHAGIA AND DYSMENORRHOEA IN CASES OF INTESTINAL DISEASE.

Schwab points out that medical treatment frequently cannot be carried out during menstruation. To shorten lengthy menstrual periods, he em-

ployed "menostaticum" (Temmler) in 120 cases of gastritis, enteritis, colitis, cholecystitis, and similar diseases. In cases of menorrhagia the periods were reduced in duration by two days. Normal periods were generally shortened by one day. Dysmenorrhoea was, as a rule, lessened in severity. The author states that the drug was well tolerated, even in cases of gastritis.

THE OPERATIVE TREATMENT OF NON-PUERPERAL PELVIC INFLAMMATORY DISEASE.

The author states that operation should not be performed in cases of recent acute attacks of adnexitis. Conservative treatment must be employed. Operative treatment is reserved for the sequelae of inflammation. He recommends Pfannenstiel's transverse abdominal route. As the disease itself is not a danger to life, the operative mortality should be nil. So far as inflammatory spread is concerned the prognosis is worst in gonorrhoeal cases. The incision of pyosalpinx and tubo-ovarian abscess is now very rarely done. It should only be necessary if the tumour is firmly adherent to the abdominal wall or to the vagina, and if evacuation of the pus is indicated by the general health of the patient. Fistulae frequently persist in these cases. The author recommends the procedure of Little and Drewitt in large adnexal inflammatory swellings. Pus is aspirated through a large needle and a solution containing 10 per cent of turpentine oil is injected into the sac. The puncture is sutured by thin catgut. Good results are obtained.

The ovaries should always be treated as conservatively as possible. All raw surfaces should be carefully peritonized. Sub-total hysterectomy is not advisable in inflammatory disease of the adnexa. In young women who are desirous of pregnancy, every effort should be made to retain the Fallopian tubes or one Fallopian tube if permeable. The permeability of the Fallopian tubes should always be tested during operation.

Albert Sharman.

Acta Obstetrica et Gynecologica Scandinavica.

Vol. xiv, Fasc. 3.

*Contribution towards the question of the diagnosis of chorion-epithelioma malignum. Otto Gröne.

A case of paratyphoid infection of a cyst of the corpus luteum. Rolf Kaijser.

Investigation into the applicability of some hepatic functional tests in pregnant women and maternity patients. Karl Lehmann.

*The necessity of strict isolation of septic cases. Sam Clason.

Does the microscopical diagnosis afford prognostic guidance in cervical cancer? Per Wetterdal.

Prolan investigations in emesis and hyperemesis gravidarum. Herman Anker and Per Laland.

Plastic operation for vaginal defect *ad modum* Kirschner-Wagner. Michael Nielsen.

*Two cases of endometriosis externa extraperitonealis. Micheal Nielsen.

Contribution Towards the Question of the Diagnosis of Chorion-epithelioma Malignum.

Gröne describes the case of a primiparous patient who passed a vesicular mole spontaneously; the uterus was curetted two days later. Luteal cysts, each the size of a fist, were felt at this time, and gradually disappeared at the end of the month. The uterus remained enlarged and a blood-stained discharge persisted. Examination of curettings obtained at this time led to a suspicion of chorion-epithelioma; the Aschheim-Zondek reaction was strongly positive. Expectant treatment was adopted for two months, and at the end of this time the uterus was a little larger but freely movable. Renewed curetting gave the same result, and injection of this material into mice gave a positive result. The Aschheim-Zondek reaction was still strongly positive.

The patient was treated by hysterectomy and a typical chorion-epithelioma was found on the anterior wall of the uterus. The writer points out in connexion with this case the importance of the Aschheim-Zondek reaction in vesicular mole and chorion-epithelioma, and describes the titration method in these cases: 50,000 mouse-units per litre will make the diagnosis suspect, and the suspicion becomes stronger as the titre rises towards 200,000 per litre. The qualitative and quantitative examination on particles of tissue obtained by excision or curetting as recommended by Zondek is also described, and Aschheim's objections on this point are discussed. Clauberg's method with infantile rabbits is mentioned.

The hormonal origin of the luteal cysts is stressed. The importance of the Aschheim-Zondek test for the clinical control of patients after the expulsion of a vesicular mole is discussed. The importance of a negative result to the test in doubtful cases in which the microscopical findings are suspicious of chorion-epithelioma is referred to and illustrated by a case of the writer.

The Necessity of Strict Isolation of Septic Cases.

Clason has undertaken a review of the number of septic cases following delivery and those following abortion at the lying-in hospital at Södra Barnbordshuset of Stockholm with their respective mortalities. The writer refers to the rapid increase of cases of abortion in proportion to full-time deliveries. In 1929 one case of abortion was admitted for each three full-time deliveries. He finds that the maternal mortality from sepsis increases with the increase of abortion.

The author finds support for the view that cases of septic abortion cannot be treated in the lying-in hospitals without occasioning a certain danger to the lying-in women, at least if conditions do not allow complete isolation of the septic cases.

Two Cases of Endometriosis Externa Extraperitonealis.

Nielsen describes two cases of endometriosis. One was in the vagina and and the other in the round ligament. After referring shortly to the different theories which have been advanced in explanation of the origin of these tumours such as the embryonal, the sero-epithelial, the metastatic and the implantation theories, he favours the last-named as giving the most con-

vincing support to the genesis of the endometriosis; because, if this condition is a disease *sui generis,* it is logical to assume a common uterine origin.

The vaginal case he explains by implantation of endometrial particles into a vaginal wound at menstruation. He attributes endometriosis of the round ligament to the deposition of endometrial particles in a pre-existing *processus vaginalis* and spread from there to the round ligament, where it becomes established while disappearing from the serous surface.

R. H. B. Adamson.

Aristencia

(The official organ of Public Beneficence in the Federal District of Mexico).

This first volume of this new journal contains articles on a wide variety of social as well as medical problems; the object of the periodical being to improve the conditions of life in Mexico by disseminating knowledge of the past and future work of the social and medical services.

An abstract of an article on "Compulsory Sterilization" by Hirschfeld follows

Compulsory Sterilization.

During the first six months of Hitler's government a law relating to "Compulsory Sterilization of the Unfit" was framed, and came into force on January 1st, 1934; 1,700 Medical Tribunals and 77 Courts of Special Appeal were created in the Reich, with the mission of pronouncing decrees relative to sterilization. According to preliminary calculation the number of individuals who ought to be sterilized was 400,000. Subsequent computation raised the number to 1,000,000 (*circa*). The surgical intervention decreed was vasectomy, which only suspends genital activity. Eight pathological conditions came under the law: (1) Mental debility. (2) Mental perturbation, e.g. schizophrenia and *dementia praecox*. (3) Hypochondria. (4) Epilepsy. (5–8) The remaining classes comprise chorea, hereditary blindness, deaf-mutism, sexual degeneration, etc.

Hirschfeld points out the technical difficulties in determining gradations in many of these conditions, e.g. Van der Tubbe, the Reichstag incendiary, was considered a schizophrenic by some of his judges, and perfectly sane and normal by others. Also many men of genius may be epileptic. "What would have become of Mahomet, Napoleon, and Dostoievsky if the law of sterilization had been enforced in their time?" It is curious that the German law neglects to recognize inveterate alcoholism as an indication for compulsory sterilization. Yet is is largely responsible for epilepsy in succeeding generations. There is also no explicit reference to criminals, contrary to North America in which several States enforce the sterilization of habitual criminals.

Actually the directors of German prisons can insist on the sterilization of criminals, who should really be in a lunatic asylum and not in a penitentiary.

A new law decrees castration of criminals guilty of "offences against

good customs." Under this category come "mixed unions," e.g. Aryans who marry Jews.

Hirschfeld gives an account of visits to North American centres of sterilization, and refers to eugenic societies in England, and to Leonard Darwin's vote of censure: "The word eugenics must not be used to justify race hatred."

In conclusion, Hirschfeld says that long before Hitler's advent to power Germany possessed institutions which aimed at solving grave problems of reproduction and heredity. A bureau for consultation regarding matrimony was opened in Berlin in 1919, and quickly thereafter 200 similar bureaux were opened in 200 German and Austrian cities. Hitler closed these, but from experience gained in them Hirschfeld thinks they offer a more prudent and efficacious preventative against catastrophies in marriage and fatal consequences to descendants. No attack is made on the liberty or dignity of the individual—which may occur in enforced sterilization—and the future generation is sufficiently protected, without recourse to arbitrary coercion.

J. H. Filshill.

Maternity Hospital, Buenos Aires, 1934

*Medico-legal considerations regarding Caesarean section post-mortem or on a dying patient. Valentinuzzi.

MEDICO-LEGAL CONSIDERATIONS REGARDING CAESAREAN SECTION POST-MORTEM OR ON DYING PATIENT.

Valentinuzzi considers medico-legal views on Caesarean section performed *in extremis*. Recently he has been interested in two cases—one attended by Olivera in 1932, the other by himself in 1933. Both patients were in the early thirties, and fell victims to double lobar pneumonia almost at term. In both there was delayed and deficient treatment before removal to hospital, where every possible remedy was tried in vain. In the first case the husband had come to hospital; he first refused to give his consent to Caesarean section, but later consented, when too late to save his wife's life. In the second, the operation was performed immediately without consultation. The child was delivered asphyxiated.

Valentinuzzi holds that one must never wait for consent to operate when the patient is in hospital and the relatives are absent. At home, consent of the father or other relatives in the house should first be asked.

He reviews the ancient (including mythological) and modern history of post-mortem Caesarean section, giving instances such as Pliny the Elder's story of Julius Caesar's birth. From remote antiquity till A.D. 1500 the operation was carried out solely on the dead, subordinate in the Roman era to a moral end, and in the Christian era to a religious one. The Popes, Paul IV and Benedict XIV, decreed that Caesarean section should be performed on the dead, that a child extracted alive should be immediately baptised, but if dead should not be buried in consecrated ground. After 1500, Caesarean section on the dead lost its religious character and became essen-

tially obstetric. In modern times, Trongé, who has studied the question extensively, gives his decision without hesitation: "I should not delay a second in carrying out Caesarean section on a pregnant woman who has just died and when the child is alive and viable." He says further that in an urgent case even a midwife might be authorized to deliver the child by post-mortem Caesarean section.

Valentinuzzi quotes from law enacted in Roman Jurisprudence, also from the present civil codes of Austria, Prussia, and the Argentine. He holds that post-mortem Caesarean section compromises no one's life, though sentimental prejudice may be against it. He agrees, however, with Brouardel: "In cases of suicide to hide dishonour there should be no intervention. The last wish of the dead should be respected." The present laws of jurisprudence consider the operation in reference to the dying as well as the dead. Caesarean section in the dying comes under the "Law of Necessity" (Jimenez de Asua) (Notricht of German Codes) and the State of Necessity ("Nothstand") excludes criminal responsibility. The foetus may live only five to 15 minutes after the mother's death—rarely 30 minutes (cases of Tarner and others). Therefore in eclamptic coma or any dying agony in which the mother is doomed, Trougé advises an ante-mortem operation. The husband's consent should be obtained in writing, to which the signatures of witnesses and of the doctors present should be appended. Each doctor should have a copy of the consent.

Valentinuzzi's final conclusion is that neither poverty of the father nor a possible toxic or syphilitic condition of the child should prevent its life being saved. "In the interests of society and the species—and according to the theological dictum—intervention is absolutely justified, whether the child turns out useful or useless, superior or degenerate."

J. H. Filshill.

The Japanese Journal of Obstetrics and Gynaecology

Vol. xvii, No. 3, June 1934.

A histological study of the cartilage of the lower end of human femur in every foetal stage. E. Terada.

Histological study of cancer in the human being. Part II: On abnormal cell-division. T. Ota.

Ovulation and oestral haemorrhage in dogs. T. Ota.

Polyovular follicles in dogs. T. Ota.

*A study on birth control with an intra-uterine instrument. T. Ota.

Investigation of the ferments in uterine cancer. Part I: Amylase in uterine cancer. K. Nakahori.

*Clinical experience with the ovarian follicular hormonal preparation "pelanin" in cases of uterine hypoplasia. Kosake and Ohgu.

Study of *icterus neonatorum*. Part IV: Haematopoietic organs and the so-called "Ikterusbereitschaft" of the human foetus. Part V: Histological findings of the haematopoietic organs and jaundice in the human newborn. H. Fujimori.

Vol. xvii, No. 4, August 1934.

Influence of the albino-rat's body fluid in deficiency-disease of vitamin B upon the continuance of the vitality of spermatozoa. J. Ueno.

Deficiency of vitamin B and the endocrine glands of female white rats. J. Ueno.

*A clinical observation on the early detachment of the normally situated placenta. A study on the treatment. Y. Katsu and H. Yamamura.

A cytological study of the living body irradiated with a hard ray. Part I: Influence of a hard ray upon the development of beans and the abnormality of the nuclei and cell-division. T. Saito.

A study of appendicitis in gynaecology. K. Mitsui.

*An experiment of lead-poisoning in pregnancy. K. Mitsui.

A functional biological study of the statistics of ectopic gestation. N. Kawashima, S. Tsuneoka, and Y. Ebara.

A Study on Birth Control with an Intra-uterine Instrument.

Several experiments have been carried out by the author to determine the efficiency of a contraceptive metal spiral ring, which has been designed by him. This ring was inserted into the uterus of a rabbit, being tied to the uterine wall with silk thread. Within a week of insertion no pregnancy ensued in the uterine cornu where the instrument was present. After a lapse of 20 days it was found that pregnancy was still impossible here, although it was possible in the other parts. Gold, silver, silver plated with gold, and brass plated with gold, were all used, and the same result obtained in each case. Premature delivery and abortion were practically negligible in their occurrence, there was not any marked changed in the uterine mucous membrane, and no inflammation.

The "Presear-Ring," designed by the author, has a hollow flat ball in the centre which is connected with the ring. The ordinary size is 18 millimetres in diameter, but this is varied according to the width and shape of the uterine cavity. One single spiral of the ring coil is 2.3 millimetres in diameter and the wire 0.3 millimetre in diameter. The ball is 7 to 9 millimetres in diameter, 4 millimetres in thickness, and about one gramme in weight.

Experimenting with this ring and the Graefenberg ring, the former was found to be superior to the latter. Using the Graefenberg ring pregnancy occurred in five cases out of 51, while with the author's ring it occurred only once in 73 cases.

The uterine mucosa showed proliferation of glands in some cases, after insertion, but generally speaking underwent no marked changes, and never any inflammatory changes. After removal of the ring pregnancy is possible. The best material for the construction of the ring was found to be silver plated with gold.

C. D. Read.

Clinical Experience with the Ovarian Follicular Hormonal Preparation "Pelanin" in Hypoplasia Uteri.

The basis of sex hormonal therapy is the characteristic effect experimentally produced on animals, usually rodents. But human hormonal relations

are much more complicated and sensitive, especially in the genital sphere. Therefore the time factor and dosage of preparations of hormones employed must be carefully regulated. In this connexion the authors refer to previous clinical investigations by Professor Okabayastir and themselves.

Their present communication concerns 32 cases of uterine hypoplasia, which have been treated by the ovarian hormonal preparation "Pelanin" (a proprietary preparation manufactured by Messrs. Shionogi and Co.) always over seven days. Before employing it, the Allen test for determination of positive hormonal content was made. The clinical results are described and arranged in nine tables, showing the number of cures in amenorrhoea, dysmenorrhoea, and irregular menstruation with or without the subsequent occurrence of pregnancy.

Experimentally and clinically it has been found that pelanin chiefly influences the uterine mucosa and the pelvic blood-supply. Along with the increase in the pelvic circulation the patient notes a feeling of warmth in the lumbar region and the lower limbs. In most cases the uterus enlarges, but, contrary to what occurs in animals, this is not permanent. Whether uterine development is entirely due to the hormones is doubtful since is was found that the excretion of follicular hormone in normal urine was the same as in cases with uterine hypoplasia. As in experiments on animals, tension of the breasts was often a consequence of the administration of pelanin. The authors conclude that (1) after comparison of the 32 cases under treatment, in those which received pelanin for two months or longer, the best effects occurred in dysmenorrhoea and the next in sterility. Improvement in cases of irregular menstruation, scanty menstruation, and sterility was also marked. (2) The effectual mechanism of the preparation seems to be reconstruction of the uterine mucosa and increase of the pelvic blood-supply. The therapy is, therefore, indicated in cases of dysmenorrhoea and sterility even when no underlying hypoplasia uteri has been detected.

A daily subcutaneous injection of 200 m.e. is the best method of treatment and dosage. This should begin post-menstrually and continue till a few days before the next period. In certain cases a larger dose can be given in one injection, but not directly before menstruation lest the cycle should be delayed. (4) According to the authors' experience the dose may be maintained constant. There is some difference of opinion between Zondek and the Dutch School as to this. The former increases the dose after menstruation up to the fifteenth day. Schroeder and others increase the dose during the second half of the post-menstrual interval. (5) No complications occur during pelanin therapy.

J. H. Filshill.

A Clinical Observation on the Early Detachment of the Normally Situated Placenta. A Study on the Treatment.

Abruptio placentae is an acute condition which instantly becomes serious. Therefore treatment must be rational and immediate, but varied according to the clinical symptoms. In this series, cases were divided into two groups, serious and slight, the former comprising patients in an acute anaemic state, and the latter cases in which haemorrhage was present, but without constitutional signs. In cases which were not serious conservative treatment was

employed, but in all other cases radical treatment was found to be necessary, and the simplest course was Caesarean section. Supravaginal amputation was used when the bleeding was very severe and when it was necessary to prevent the loss of more blood.

AN EXPERIMENT OF LEAD-POISONING IN PREGNANCY.

The author caused 94 pregnant rabbits to be poisoned by lead, and a short time afterwards carried out an investigation to compare the relation between the distribution and the histological changes in the tissues of the different organs, to ascertain how lead-poisoning disturbed the pregnancy. The fact that intra-uterine death or stillbirth occurred was due to the direct action of the lead which was first transported into the foetal body and was then deposited in the different tissues. Marked deposits of lead and morbid changes were present in the placenta.

C. D. Read.

REPORTS OF SOCIETIES

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

A meeting of the Society was held at Liverpool on Friday, October 26th, 1934, with the President, Professor DANIEL DOUGAL (Manchester) in the chair.

The PRESIDENT described the after-histories of two cases operated on by him.

1. A CASE OF ROUND-CELLED SARCOMA OF THE UTERUS.

In the first case he removed an apparently fibroid polypus from a woman nine weeks post-partum. Microscopically it was a round-celled sarcoma, and he accordingly did a total hysterectomy: this was in July 1933. He saw the patient again in August 1934, when she complained of pain in the left side and soreness about the vulva. There was a growth the size of a walnut near the urethra. The vulva was excised, and deep X-ray therapy given. When seen recently she was dying, with a mass in the iliac fossa and haemoptysis. The opinion had been expressed in the Society that hysterectomy was too radical a measure.

2. ACUTE INTESTINAL OBSTRUCTION FIVE YEARS AFTER BALDWIN'S OPERATION.

The second case was that of a patient on whom the President had done Baldwin's operation for the construction of a vagina five years ago. At the time of operation the patient was aged 22 and single but about to marry. She had now been married four years, and marital relations were satisfactory. She had an attack of acute intestinal obstruction in February 1934, and underwent operation: a band was the cause of the obstruction. On recent examination the intestinal mucosa lining the vagina was seen to have changed to a greyish-pink colour. There was a profuse mucous discharge from it, but otherwise no trouble was caused.

Mr. P. MALPAS (Liverpool) described

A CASE OF HYPERSEXUALITY ASSOCIATED WITH CYSTIC OVARIES AND TREATED BY PARTIAL OÖPHORECTOMY.

The patient, a girl aged 23, was referred to me by her doctor on account of insistent and uncontrollable sexual irritability. This was in the main

attributable to the girl's previous life. She was brought up in the most unfortunate of homes, had a child at the age of 16, and thereafter lived on the streets until the age of 22, when, because of soliciting, she was placed on probation in an institution. In the institution she proved a good worker and seemed quite contented, but continued sexual irritability proved not only a source of distress to herself but a problem to the authorities. She was seen by a psychologist, who reported that she seemed a normal girl mentally, particularly in view of her previous life.

On examination she proved to be a well-built normal girl. Physical examination revealed nothing abnormal beyond bilateral enlarged but mobile ovaries. In the hope that the ovarian change might be the cause of the undue sexual irritability I explored the pelvis. Both ovaries proved to be enlarged, each being about two and a half inches long by two inches wide. The enlargement was seen to be due to the presence of innumerable follicular cysts, none larger than gooseberries, mostly of the size of peas. In addition to the ovarian change a marked varicose condition of the pampiniform plexus was present on either side, the constituent veins having the diameter of a fountain-pen.

I resected the cystic portion of both ovaries, leaving about one-fourth of each organ. In addition ligatures were placed around the more prominent veins of the varicoceles. Sections of the ovaries show an excessive number of both primordial and developed follicles and an excess of granulosa cells as compared with a normal organ. The patient made a satisfactory recovery and her doctor reported three months after the operation that she had settled down well and that the sexual irritability was no longer a trouble.

The case is interesting in showing a definite overproduction of mature follicles as the result of long-continued excessive sexual stimulation. The girl's hypersexuality can be explained by the excessive stimulation caused by an undue number of follicles ripening simultaneously. In other words, the case was treated during the second phase of a vicious cycle. Resection of the hypertrophied ovaries permitted the re-establishment of a normal level of sexual function.

It is acknowledged that among the more important effects of the sex hormones is their mental effect. Everyone who has used oestrin in cases of functional amenorrhoea, or in an attempted therapeutic abortion, must have noticed that often the only effect of the injections has been the production of the mental impression of an impending period.

In this regard the instance of a case of epilepsy which I have seen recently may be relevant. The epilepsy commenced two years after puberty and was associated with irregular menses. Intensive medical treatment failed to control the fits, which were definitely those of true major epilepsy, but partial resection of cystic ovaries, similar to those described in the former case, immediately terminated the incidence of the fits. In this case, too, there was some mental instability.

Dr. J. W. Burns (Liverpool) cited a case of epilepsy in which removal of an ovary had been followed by progressive deterioration of the patient.

Dr. M. M. Datnow (Liverpool) thought that the pituitary gland was

possibly the cause of the trouble; he suggested that antuitrin-S was indicated, to promote luteinization.

Professor LEYLAND ROBINSON (Liverpool) drew attention to the facts that most epileptics have their fits during the period, and that suicide, when occurring during sexual life, usually occurs at the period. In cases of this type he advocates deep X-rays, in the first instance to one side only.

Dr. J. W. BRIDE (Manchester) described

A CASE OF ADVANCED CARCINOMA OF THE CORPUS UTERI AND VAGINA.

This case, which appears to have some points of interest, is one of squamous-cell carcinoma of the vagina and adeno-carcinoma of the body of the uterus.

The patient, E.S., aged 57, had been married 33 years and had three children and two miscarriages. She consulted me in February 1934, complaining of irregular bleeding and watery discharge after the menopause, which occurred at 38 years of age—that is, 19 years ago. Two years after this she had slight bleeding, and again two years later a repetition of the bleeding. During the last three years she had irregular haemorrhage for an hour or so at a time, at intervals of a few months, and continuous bleeding for the past week. There had been no abnormality on micturition or defaecation. Her general condition was fair, and she had no pain.

On examination I found a hard plaque of tissue about an inch long and half an inch wide on the posterior vaginal wall, just within the vaginal orifice. The uterus was anteflexed and enlarged to the size of an eight-weeks' pregnancy. The vaginal tumour was fixed and bled on touching. I made a diagnosis of cancer of the vagina, and suspscted malignant disease of the body of the uterus. On February 12th the patient was anaesthetized, and I excised a piece of the vaginal growth, which penetrated deeply into the recto-vaginal septum. I dilated the cervix, curetted the uterus, and removed obviously carcinomatous material. Microscopic sections showed squamous-cell carcinoma of the vagina and adeno-carcinoma of the uterine body. I decided to treat the case with radium, and on February 15th I inserted 75 milligrammes into the uterus and 35 milligrammes into the vagina for 22 hours. This treatment was repeated on February 22nd and March 19th.

On her return home she steadily improved for a time, and bleeding and discharge ceased until July, when I was asked to see her on account of purulent discharge, and I found pyometra, which I drained. The vaginal growth had completely disappeared, but the uterus was larger and fixed with masses in both iliac fossae. When I saw her a month ago the condition was the same, except for advancing emaciation.

The co-existence of adeno-carcinoma of the corpus uteri and squamous-cell carcinoma of the lowest part of the vagina, with no apparent continuity between the two, is rare. Cullen,[1] in *Cancer of the Uterus*, states that "were we to find a squamous-cell carcinoma of the cervix and an adeno-carcinoma of the body or the converse . . . we might consistently speak

of two carcinomatous processes occurring independently of each other." This seems to me to apply much more forcibly to two processes separated by two-thirds of the vaginal canal.

Eden and Lockyer,[2] in their *Gynaecology*, say that "growths secondary to carcinoma of the uterine body sometimes occur in the vagina from direct implantation of cancer cells carried down from the uterus in the discharge." In such a case the vaginal growth should be adeno-carcinoma, as in a case described by Cullen.[3] In my patient the vaginal growth is obviously squamous-cell carcinoma, and so I am inclined to consider the two growths as independent.

Another point is that carcinoma of the uterine body generally develops in older patients and some time after the menopause. My patient was 57 years of age, but the menopause commenced at the early age of 38 years, so that in this respect she conformed to the rule.

For the treatment of carcinoma of the uterine body I consider total hysterectomy preferable to radium, but the presence of the advanced vaginal growth seemed to contra-indicate this. The ready response of the vaginal squamous-cell growth to radium, and the failure of any response to such treatment of the uterine growth, confirms the advisability of removing the uterus if possible.

In conclusion, I should be glad to know if the two growths are to be regarded as independent, and if other members have encountered a similar case.

The PRESIDENT had seen several cases of secondary adeno-carcinoma of the vagina with the primary growth in the uterine body: he regarded them as cases of gravity implantation.

Professor W. GOUGH (Leeds) thought that such secondary deposits were sometimes due to lymphatic spread; he had seen a case in which the nodules of growth had been submucous, lying beneath a normal vaginal mucosa.

Mr. J. E. STACEY (Sheffield) thought that on anatomical grounds the lymphatic theory was untenable. He suggested that the vaginal growth in this case had undergone squamous metaplasia.

References.

1. Cullen, T. S. *Cancer of the Uterus*, 1900, p. 594.
2. Eden, T. W., and C. Lockyer. *Gynaecology*, 1928, p. 483.
3. Cullen, T. W. *Ibid.*, p. 415.

Dr. C. H. WALSH (Liverpool) reported

A CASE OF ACTINOMYCOSIS OF THE OVARY.

The patient was aged 26. For several years she had not felt well, and often had pains in the abdomen. She had a normal pregnancy and confinement in 1930. For six months she had complained of dysmenorrhoea, with scanty menstruation; leucorrhoea, with brownish intermenstrual

vaginal discharge; occasional attacks of severe pain in the lower abdomen, sometimes associated with vomiting; constipation; general weakness; wasting; loss of appetite; night sweats.

Examination on January 26th, 1934.—The general condition was poor; the mucous membranes pale; the temperature and the pulse-rate were normal.

Vaginally there was a palpable mass in the right fornix attached to a bulky tender uterus.

Diagnosis.—A diagnosis of tubo-ovarian abscess was made.

Treatment.—The abdomen was opened on February 2nd, 1934. A right-sided tubo-ovarian abscess, about the size of a grape-fruit, was found in the pelvis. Attached to it was an inflamed thick red appendix, omentum, and several loops of small gut. The caecum appeared to be normal. The abscess burst during removal, and discharged foul-smelling pus. The adhesions of gut and omentum were separated, and the right Fallopian tube, right ovary and the appendix were removed. The left Fallopian tube and ovary seemed to be perfectly normal and were conserved. Her convalescence was uneventful, and she was discharged in three weeks. A section of the removed tissue showed the tube to be very vascular, with oedema of the muscle, the lumen containing pus, and subacute suppurative changes in the mucosa. The ovary showed well-marked subacute inflammatory changes.

Further history.—A menstrual period began on March 28th; did not menstruate in April, but on May 18th had a period lasting six days, which began one week early. Then she had a daily show until June 6th. Her last period was on June 28th, lasting five days. For four weeks prior to re-admission to hospital, on July 16th, she had continuous pain in the lower left abdomen, sometimes associated with vomiting.

Condition on Re-admission.—On examination vaginally she had a mass in the left appendage, which was diagnosed as a left tubo-ovarian abscess.

Operation on July 20th, 1934.—There were a few filmy adhesions of omentum to the scar in the abdominal wall. The pelvis was occupied by a left tubo-ovarian abscess to which loops of small gut, sigmoid colon and rectum were firmly attached. After separation of these adhesions the appendage was mobilized and removed entire. The loop of gut firmly attached to the posterior surface of the uterus precluded hysterectomy. Another loop of gut was so firmly adherent in the lowest part of the pouch of Douglas that separation was impossible. Realizing that intestinal obstruction would be the inevitable outcome of these adhesions, an ileo-ileostomy was performed leaving about two feet of ileum adherent in the pelvis.

Convalescence.—This was peculiar. The temperature remained normal until the ninth and tenth days, when it reached 100.4°F., but it has been normal since. The pulse-rate averaged 90 per minute. She felt tired and listless, and became very pale and emaciated. The wound discharged some foul pus on the fifteenth day, but healed later. Her red blood-corpuscles numbered 3,000,000, white blood-corpuscles 13,200, haemoglobin 45 per cent, colour index 0.7. A pint of Group IV blood was given four weeks after operation. This improved her condition enormously, and later the blood

count was: red blood-corpuscles 3,980,000, white blood-corpuscles 25,800, haemoglobin 60 per cent, colour index 0.8. A mass—not tender—appeared in the right iliac fossa, associated with persistent vomiting and severe abdominal pain. Intestinal obstruction with a residual abscess was thought to be the diagnosis, and her condition was critical. Then the pathologist, Dr. H. Osborn, reported on the section. By great good fortune a section was taken through that particular part of the wall of the tubo-ovarian abscess which contained actinomycosis.

Section.—Many other sections have been taken from the specimen, but this is the only block in which ray fungus was demonstrated. It is apparently *actinomycosis bovis.*

Treatment.—She was immediately given iodine in milk three times daily with most marked improvement generally and locally. There is now no mass palpable abdominally, and her general health is better. The lower angle of the wound discharges pus occasionally but actinomycosis has not been demonstrated in the discharge. She complains of pain in the left hypochondrium. A radiograph showed thickened pleura at the left base. There is no mass palpable in the splenic area.

Comments.—Actinomycosis of the appendages is a very rare condition. Arthur Stern in 1928 reported 43 cases in the literature. He concluded that in the majority of cases the origin is from the intestine, especially the caecum, and that it is very doubtful if the streptothrix may reach the ovary via the vagina. Graves in 1928 thought that actinomycosis of the internal genitalia was commoner than is supposed. Infections of this type are overlooked owing to the fact that only in certain cases do the microbes have the typical radial grouping of a ray fungus. In this case there is the possibility that the infection may have passed from the appendix into the right appendage, which was thought to be a simple chronic inflammatory lesion, and later the left appendage became affected and its true nature fortunately discovered on section.

Abdominal actinomycosis has a grave prognosis, and usually ends in death from cachexia and secondary anaemia, with the formation of multiple sinuses. Blood transfusion and the giving of iodine has obviously helped this patient, but time alone will show whether the improvement can be maintained.

Professor W. Gough said that clubs were rarely seen in man. He asked whether the patient kept hens or pigeons?

Dr. Walsh replied in the negative.

Dr. C. H. Walsh (Liverpool) showed

A Specimen of Chorion-epithelioma, following Ectopic Gestation.

The patient was aged 42 years.

Past history. She had been pregnant 10 times; the first, second, third, and fourth pregnancies ended in full-time normal labours between 1914 and 1920; the fifth pregnancy ended in abortion at the third month; the sixth, seventh and eighth in full-time normal labours between 1925 and 1930; the

ninth terminated in abortion at the third month in 1931; and the tenth in abortion at the third month in February 1933.

Present history. Her menses started again in March 1933, and were regular and without pain, cycle 7/28, until October 15th, 1933. She missed the November period, and had a slight loss for two days in mid-December. There had been no vaginal haemorrhage since. Six weeks prior to admission to hospital she commenced to have pain in the right lower abdomen, which had persisted more less continuously. On the day previous to admission she had a severe attack of abdominal pain and vomited. Only then did she call in a doctor, who advised immediate admission to hospital.

Condition on admission. The bowels were constipated; there was no difficulty in micturition, and no discharge vaginally. She stated that she had had weaknesses since her miscarriage in February 1933, but that she had been gradually getting paler since January 1934, and had fainted on several occasions recently.

Examination on February 27th, 1934.

General condition. There was a severe degree of anaemia, the mucous membranes being definitely blanched. There was no pyrexia; pulse-rate 98 per minute. She was well nourished and of cheerful disposition.

Cardio-vascular system. No bruits were detected in the cardiac area.

Blood examination. This revealed the following findings: Red blood-corpuscles 3,140,000, white blood-corpuscles 9,000, haemoglobin 46 per cent, colour index 0.74.

Differential count. Polymorphonuclear cells 7,074, 78.3 per cent; large lymphocytes 279, 3.1 per cent; small lymphocytes, 1,458, 16.2 per cent; eosinophiles 54, 0.6 per cent; mast cells 162, 1.8 per cent. A secondary anaemia was the obvious picture. Her blood was Group IV.

Nervous system. No abnormality was detected.

Respiratory system. She had no cough, but a few scattered rales were heard over the bases of the lungs posteriorly.

Alimentary system. The teeth were carious and pyorrhoea present. There was no distension of gut, and no physical signs to suggest that the alimentary tract was involved.

Urinary system. No dysuria. *Urine*: Reaction acid; a slight trace of albumin was found; no sugar; no acetone. Microscopically there were no abnormal cells.

Abdominally. A tumour extended from the pelvis to the level of the umbilicus. It had the appearance and feel of a 22-weeks' pregnant uterus, displaced slightly to the right of the middle line. Its surface felt smooth, its contour was regular, and its consistence soft. It was not movable. Neither foetal heart-sounds nor uterine sounds were heard. The abdominal wall was relaxed, and she did not have abdominal pain at the time of examination. There was slight tenderness only on deep palpation in the iliac fossae.

Vaginally. There was no discharge or haemorrhage. The perineum was deficient. The cervix, normally situated, felt slightly softened. It

could be moved through a wide range without any movement of the tumour. The body of the uterus could not be differentiated from the mass.

Diagnosis. A diagnosis of secondary abdominal pregnancy with haemorrhage was made.

Treatment.

A transfusion of 295 cubic centimetres of blood was given by the direct method using a Jubé syringe. A rigor with a temperature of 101.4°F. occurred the same evening, but the pulse-rate remained steady at 110 per minute. Her colour improved enormously and she felt much better. A sound passed into the uterus easily and demonstrated that the body was lying alongside of and to the left of the tumour. The cavity was of normal depth, two and a half inches, and apparently intact. When the sound was removed a slight amount of tarry blood escaped from the uterus. Three days later, under ether anaesthesia, the abdomen was opened through a midline supra-pubic incision. Immediately the peritoneal cavity was reached a great quantity of old, dark, free blood and blood-clot appeared. The tumour was a dark blood-coloured mass arising from the vicinity of the right cornu of the uterus. The following structures were attached to it: below and in front, the bladder; above and in front, two loops of small gut and omentum; below and posteriorly, the sigmoid colon; to its left, the uterus; to its right, the caecum. These structures were separated readily enough, but free bleeding occurred from the mass at the sites of detachment. The patient collapsed from haemorrhage during the separation of the adhesions. A rapid sub-total hysterectomy with removal of the Fallopian tubes, ovaries and mass *en bloc* was performed. The abdomen was quickly closed and a submammary saline infusion started. She died half an hour after operation. A post-mortem was firmly refused.

Specimen. Weight, 26 ounces; dimensions, eight inches, by three inches, by five inches.

Microscopically. The uterus is of normal size. In the right side of the fundus there are several haemorrhagic nodules, adjacent to the mass.

After fixing, the uterus was opened along its anterior wall. Its lining surface is white and everywhere intact. There is no growth within the cavity of the uterus. At the right cornu the muscular wall is necrotic and haemorrhagic. Both the ovaries are small and do not show macroscopic evidence of theca lutein cysts. The left Fallopian tube is normal. The fimbriated end of the right tube is easily distinguishable, and a portion of the ampulla of the tube can be traced into the tumour. A probe can be passed along the tube into the mass. The mass is haemorrhagic, friable and solid. It appears to arise from the right Fallopian tube, and is invading the right cornu of the uterus to which it is attached. The right broad ligament is attached to the uterus.

Microscopically. Sections of the periphery of the tumour show blood clot only. Sections from the right cornu of the uterus show that the endometrium is intact, and is represented by a layer of stroma-cells and glands. There is no decidual reaction. The muscle is infiltrated with chorion-epithelioma. Langhans's cells are seen in profusion; there are a few multinuclear cells but no villi. Haemorrhage into, and necrosis of, the

muscle is in evidence. It is apparent from the section that the growth is invading the uterus from without inwards.

Comments. This is a case of chorion-epithelioma following an ectopic gestation in the right Fallopian tube. It is a rare condition.

Szathmary collected 1,412 cases of chorion-epithelioma and found that 6.6 per cent followed ectopic gestation. In Pollosn and Violet's series of 455 cases, 2.5 per cent were ectopic. In the six-year period, 1928 to 1933, at Mill Road Infirmary and Smithdown Road Hospital, Liverpool, there have been two cases of chorion-epithelioma in 10,830 pregnancies, 56 of which were ectopic, and in the same period 16 hydatidiform moles.

Mr. J. St. George Wilson (Liverpool) read a note on

The Zondek-Aschheim Reaction in Genital Tuberculosis.

The association of a positive Zondek-Aschheim reaction with genital tuberculosis was discovered by chance in one case, but the coincidence of these two conditions was proved in others, which led me to the opinion that there is some relation between them.

A single girl, aged 25, was admitted to hospital suffering from pain in the right iliac fossa and swelling in the abdomen, which she said was getting smaller. She had an attack of pain some months previously, and had been admitted to hospital for removal of the appendix, but the operation was not done. She had had an abdominal operation four years previously for supposed appendicitis, but was told that she had tuberculous glands. She had her first period at the age of 17, then 12 months' amenorrhoea, and from then to the age of 21 she had periods at intervals of two or three months. Latterly the periods had been regular, the last being a fortnight before her admission.

When I first saw her I was told that the Zondek-Aschheim test was positive. On abdominal palpation she had an indefinite swelling in the right lower abdomen. Bimanual examination revealed the fact that the uterus was in normal position with doubt about its exact size. The swelling could be felt in the right fornix as a thin-walled cyst, and there was general resistance on both sides of the pelvis. I was of the opinion that she had tuberculous disease of the appendages, for which I prefer deep X-rays to operative treatment. The presence of a positive Zondek's reaction, however, made me open the abdomen. The cyst was a thin-walled peritoneal cyst, often associated with chronic disease of the appendages, and she had obvious tuberculous masses in both appendages. I removed the right, which was the worse, and conserved the left. Microscopical examination showed the presence of tubercles in the Fallopian tube.

I saw her three months later, when she still complained of abdominal pain. She had had three normal periods. There was a small cystic swelling in the left fornix, and the report from the Pregnancy Diagnosis Station was that the Zondek-Aschheim test was negative, but suggestive of an excess of prolan. I have since put her on deep X-ray therapy.

The next patient was a girl of 19, who had a history of irregular periods for six months before admission. She had swellings of the appendages, one

on the left side extending above the pelvic brim. She was treated expectantly in the hope that her temperature would settle. The condition of her chest, though clinically suspicious, was reported radiologically as non-tuberculous. The Mantou skin test was negative. The Zondek-Aschheim test was weakly positive. We did next a posterior colpotomy, but only clear fluid under tension was evacuated. Three weeks later another vaginal exploration was carried out, and a small amount of pus evacuated. She commenced to go down hill, so we opened her abdomen and found both Fallopian tubes enlarged and thickened, and omentum and gut adherent in the pelvis. An abscess was opened in the left side of the pelvis. Both appendages were removed and the peritoneal cavity was drained. Microscopically tubercles were present in the Fallopian tubes. She died in 48 hours.

Post-mortem. The findings were those of general peritonitis. No other signs of tuberculosis were found.

The next two cases were of secondary amenorrhoea. I have long been of the opinion that tuberculosis may cause both primary and secondary amenorrhoea. One of these cases gave a history suggestive of tuberculosis. She was aged 28, and had had amenorrhoea for 18 months. She had commenced menstruation at 13 years, with cycle 7/14. She had had four abdominal operations; the first at the age of 16 for peritonitis, the second at 17 for inflammation of the stomach, the third at 19 for oöphorectomy, and the fourth at 23 for a cyst of the ovary. The uterus was small and normal in position, and there were no appendages. The Zondek-Aschheim was positive, as was also the Mantou test. Lipiodol injection showed a small fundus with absence of filling of the Fallopian tubes.

The fourth patient was a girl aged 20, who had amenorrhoea from February to August 1934. She had a normal period in February, and previous to that she had amenorrhoea since October 1933. The uterus was normal in size, and the appendages were normal. The Zondek-Aschheim reaction was positive. Treatment with antuitrin-S produced a period on October 10th, 1934.

Mrs. M.S. was aged 28, and had two children. She had been treated for phthisis and is attending a tuberculosis dispensary at present. She complained of lower abdominal pain and pelvic tenderness. The appendages were thick and tender. The last menstrual period occurred during the previous week. At operation the appendages and uterus were apparently normal; she had chronic appendicitis. The Zondek-Aschheim reaction was negative, but the urine contained an excess of anterior pituitary hormone.

Mrs. E.M., aged 20. This was a definite case of pulmonary tuberculosis, both clinically and radiologically. She had had amenorrhoea for four months. The uterus was normal in size; it was questionable whether the left appendage was thickened or otherwise. The Zondek-Aschheim reaction was negative, but showed an excess of anterior pituitary hormone.

Mrs. M.M., aged 33. The patient complained of sterility. She menstruated for one day every three months. There was a large cystic swelling to the left of the uterus, and a small swelling to the right of the uterus. At operation tubercles were found on the peritoneum. The left appendage

was removed. Microscopically, tubercles were found in the Fallopian tube. The Zondek-Aschheim reaction after operation was negative.

Mrs. O'M., aged 36. This patient had pulmonary tuberculosis and menorrhagia, associated with bilateral swellings of the appendages. She was treated with deep X-rays, which caused amenorrhoea for 12 months, followed by regular periods. The Zondek-Aschheim reaction was negative after treatment.

Summary. Two cases of proved tuberculous salpingo-oöphoritis showed a positive Zondek-Aschheim test before operation. Two cases of prolonged amenorrhoea with histories very suggestive of tuberculosis showed a positive Zondek-Aschheim test. One case with a short period of amenorrhoea with definite pulmonary tuberculosis showed a negative Zondek-Aschheim test, but evidence of increase of anterior pituitary secretion. Two cases gave a negative Zondek-Aschheim test, but showed evidence of excess of anterior pituitary secretion, with a definite history of tuberculosis, in one case positive before operation. Two cases gave a completely negative Zondek-Aschheim test after treatment; one case was treated by operation at which tuberculosis was proved, and in the other, in which tuberculosis was clinically positive, was treated by deep X-ray therapy.

Conclusions. The presence of a positive Zondek-Aschheim test is associated with tuberculous salpingo-öophoritis. The presence of a positive Zondek-Aschheim test associated with amenorrhoea when pregnancy can be excluded is suggestive of tuberculosis. The presence of a modified Zondek-Aschheim test might indicate healing or retrogression of genital tuberculosis, especially if previously definitely positive.

No information is found in medical literature dealing with this subject.

Dr. T. N. A. Jeffcoate (Liverpool) mentioned a case of genital tuberculosis with secondary amenorrhoea of seven years' duration. The patient had a cystic swelling which reached the umbilicus. The Zondek-Aschheim test showed excess of prolan A, but was not positive. Dr. Jeffcoate regards the positive result in tuberculosis associated with amenorrhoea as analogous to the positive result that may be obtained at the menopause or after radiation.

Mr. P. Malpas asked whether the positive reaction was a specific effect of the tubercle bacillus or whether it was due to destruction of ovarian tissue.

Dr. M. M. Datnow did the actual tests. He suggested that if all the ovarian tissue was destroyed the body was producing pituitary secretion which was not used by the ovary and passed out in the urine, causing a positive Zondek-Aschheim reaction. If the body uses some pituitary secretion, then the reaction is less strongly positive (excess of prolan A).

Mr. Wilson, in reply to Mr. Malpas, thought that the positive reaction was a specific effect of tuberculosis.

Mr. C. H. Marshall (Liverpool) read a short paper on

Willett's Forceps in Placenta Praevia.

The treatment of placenta praevia has exercised the minds of generations of obstetricians, and the number of measures which have been evolved to

deal with this condition suggests that no single method is applicable to all types of lower segment placental insertion. The routine methods of treatment, apart from such conservative measures as rupture of the membranes, or vaginal plugging, up to the year 1925 involved either compression of the placenta and placental site by the half-breech, or the hydrostatic bag, or consisted in direct evacuation of the uterine contents by Caesarean section.

In 1925, however, the late J. Abernethy Willett, then Obstetric Surgeon to the City of London Maternity Hospital, introduced the simple method of bringing pressure to bear on the placental site by scalp traction. Willett rightly considered that the simplest and gentlest means of controlling haemorrhage in these cases was to be obtained by rupturing the membranes and by making downward traction upon the presenting vertex. He maintained that the method involved minimal handling and consequently decreased maternal risk and increased foetal survival. For this purpose he selected Martel's scalp forceps which since that time has been modified to the present instrument which bears his name.

Since that year no large series of cases treated by this method has been published, though it is evident from the literature that the instrument has been used sporadically both in this country and abroad. This is apparent from the allusions to this method of treatment in the publications of Lacy, Barris and Jennings.

That the knowledge of Willett's forceps is not so widespread as might have been believed, is obvious from a perusal of a recent article in the *Zentralblatt für Gynäkologie* by Gauss of Würzburg, who appears to have rediscovered the principle of scalp traction. For in his contribution under the title of "a new, safe, and extremely successful method of treating placenta praevia" he merely outlines the principles enunciated by Willett. No mention is as yet made of this method in the recent American or Continental textbooks.

At the Liverpool Maternity Hospital during the years 1926 to 1931 inclusive, 170 cases of placenta praevia were treated either conservatively or by means of podalic version or Caesarean section. During this period in no case was Willett's scalp forceps used. The maternal mortality was 14 deaths, or 8.2 per cent. The foetal survival rate of the cases treated by the half breech method was nine infants in 79 cases, or under 12 per cent.

During the years 1932, 1933 and the first ten months of the present year [1934], 118 cases of placenta praevia have been treated at the Institution, with a maternal mortality of four, or 3.4 per cent, which is well under half the mortality prevailing in the survey of the previous six years.

Since 1932, however, the use of Willett's instrument has increased yearly with a corresponding decrease in the number of versions performed. In all, 30 patients were treated by scalp traction with a survival rate of 15 infants, or 50 per cent. The Caesarean section rate for placenta praevia throughout the nine years under review has ranged slightly above or below 20 per cent, but during the last three years the version rate has markedly diminished at the expense of a correspondingly marked increase in the use of Willett's method. That this has been justified is obvious from a study of the maternal mortality and foetal survival rate.

Method of application of the forceps. While the lithotomy position is desirable, it is not absolutely necessary. If the bleeding has been considerable and symptoms of anaemia are present, the thighs are simply flexed and abducted, and the instrument can then be applied in many cases with the least possible disturbance to the patient. Anaesthesia is not used in such a case, and indeed is frequently dispensed with in the multiparae. When the case is first seen in hospital after the initial bleeding there is usually no more than a steady or intermittent trickle of blood from the vagina. One can expect, however, to find a few large clots in the vaginal vault. It is essential that these should be removed and manipulations with the fingers inevitably cause further bleeding. If the patient is in the lithotomy position the gentlest way is to insert an ordinary duckbill speculum along the posterior vaginal wall. The vulval end is now depressed, and the clots readily glide out.

While an assistant fixes the head in the brim, two fingers of the left hand are passed into the vagina and one or both, according to the degree of dilatation, through the cervix. If the placenta is felt partially overlapping the internal os, a clear area is sought where only membranes intervene between the head and the examining finger. This will usually be found anteriorly, for the placenta is much more commonly found on the posterior wall of the lower segment. The membrane hook is guided along the fingers, and the membranes scratched through against the head. Without withdrawing the fingers, the forceps is similarly guided, opened, pressed firmly against the scalp, and closed. Before the fingers are withdrawn the grip on the scalp is tested by making traction. Any bleeding which the manipulations may have caused should cease immediately. The patient is drawn up the bed again, and a cord carrying a weight of one pound over a pulley at the foot of the bed is attached to the handles of the forceps. If anaesthesia has been used, it is best to control the tension with the hand until any vomiting has ceased. When abdominal and rectal examination show that the head has descended completely into the pelvis the forceps may be removed.

Comparison with version. That the foetal results by this method of treatment are superior to those obtained when the half-breech is used is probably due rather to the cumulative effect of several factors than to the isolated working of any one. In Willett's method anaesthesia may often be avoided, the manipulations are gentler, operative loss of blood and further placental separation, which it denotes, are reduced to a minimum, while the amount of liquor lost is much less than that which escapes during bipolar version. Finally, if the foetus is near term, and specially if the patient is a primiparae, the disadvantages of a breech presentation are obviated.

It must, of course, be remembered that part of the high foetal mortality following bipolar version can be attributed to the fact that this method of treatment is frequently employed in cases of central placenta praevia. There is every reason why scalp traction should displace the use of the bag. If the local conditions are such as to enable easy insertion of a bag, then the forceps may be applied with greater ease, and probably with even better results.

With a few exceptions vaginal packing need hardly be considered a

method of treatment: it is a method of infection. It has been commonly used to stem haemorrhage when the dilatation of the cervix was not sufficient to admit of treatment by methods involving the insertion of two fingers. Provided one finger plus the forceps can be passed through the os, the forceps may be applied to the scalp. As this is almost always possible, there is little justification for packing even among those who fail to realize its great danger.

Mode of action of the forceps. This method of treatment combines the advantages of simple rupture of the membranes, and the maintenance of continuous pressure on the denuded portion of the placental site. This pressure is not obtained by actually drawing down the bony cranial vault. When the forceps is applied against the most accessible part of the head and the jaws closed, a ridge of scalp is raised. If traction is now applied, a wider area of scalp is drawn out in the form of a cone, the apex of which is drawn into the internal os. In this way pressure is brought to bear on the bleeding surface and the haemorrhage is immediately checked. Doubtless, in a proportion of cases, simple rupture of the membranes is adequate treatment. Such cases can be simply distinguished by observing whether traction has to be added in order to control the bleeding. However, a weight of a pound or a pound and a half is probably always an advantage whether it seems to be required or not. Pains appear to be induced sooner if these are not already present. Unnecessary leakage of the liquor is also prevented, a factor which is surely favourable to the foetus. Further, if, when the membranes are ruptured, the forceps is applied to the scalp as a routine, it is comforting to know that traction can be applied at any moment should bleeding again occur. Undoubtedly a leg has frequently been pulled down unnecessarily in order to obviate the possibility of a second manipulation.

Indications for its use. The vertex must be presenting. Placenta praevia is not infrequently associated with breech presentations. External cephalic version can often be performed with ease, as the child is usually premature and the membranes are nearly always intact when the case is first seen. Though I have done this in one or two cases, I do not strongly recommend it.

If the foetus lies obliquely or transversely, a central insertion of the placenta should be suspected. In this variety the treatment can hardly be recommended. In a few cases in this series the edge of the placenta was torn through in applying the forceps, but in only one was the forceps passed through the centre of the placenta. Owing to the profuse haemorrhage which can accompany any vaginal method in the treatment of this variety, the mother's interests are often best safeguarded by abdominal delivery.

In absolute emergencies where the necessary local conditions are present, I should imagine it is much easier to burrow through the placenta with the fingers and grasp a foot than to attempt to fix the forceps to the scalp of a head which is unstable and perhaps only with difficulty brought to the midline. Disproportion, which is not commonly met with in these cases owing to frequency of prematurity, should be regarded as a contra-indication to this line of treatment.

Disappointments of the method. Very rarely the forceps may lose its

grip and come off before it has fulfilled its purpose. This accident can usually be prevented by carefully ensuring before withdrawing the guiding fingers that the amount of scalp grasped has completely and evenly filled the jaws of the forceps. The likelihood of the forceps tearing off is greatly increased if the foetus dies and maceration commences in the scalp. The forceps may have to be reapplied, or some other line of treatment adopted.

The other disappointments are usually due to factors which are common to most methods of vaginal delivery in this condition and over which we have no control. The foetal heart sounds, which for some hours have been strong and regular, may gradually die away. This seems to occur most often in the late first or early second stage of labour, and, unfortunately, with the more mature type of foetus. With advancing labour and increased stretching of the lower segment, so wide an area of placenta may separate, or such thinning of the uterine wall may occur as to interfere seriously with foetal oxygenization. Compression of the placenta by the presenting part itself is a possible cause of foetal death. In one case in which the cord was found to be inserted on the edge of the placenta which overlay the internal os, compression of this was apparently the cause of foetal mortality.

Conclusions. (1) Our own experience and the writings of others show that scalp traction perfectly fulfils the first and the greatest of its aims, the control of haemorrhage. (2) I think we are justified in assuming that lower maternal mortality and higher foetal survical rates will result from a wider use of this method. (3) The method is a simple one, and beginners certainly find it easier to carry out than bipolar version. (4) No attempt is made here to compare its usefulness with Caesarean section, which has its own special indications in the treatment of this condition.

Mr. Marshall showed a film demonstrating his technique.

Mr. J. E. Stacey reported a series of cases treated at Sheffield. As at Liverpool, there was more improvement in the maternal than in the foetal deaths.

Dr. J. W. Burns (Liverpool) said that he was a complete convert to the method.

Dr. E. A. Gerrard (Manchester) said that the great advantages of Willett's forceps were that it was easy to use, and applicable when there was very little dilatation of the cervix.

Mr. A. M. Claye (Leeds) expressed surprise that it was the bipolar variety of version with which the method had been contrasted. Surely the type of version associated with the minimum of manipulation and haemorrhage was external podalic version followed by the bringing down of a leg.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

The Society met at Sheffield on Friday, November 23rd, 1934, with the President, Professor DANIEL DOUGAL (Manchester) in the chair.

The PRESIDENT described a case of

A MALIGNANT OVARIAN TUMOUR REMOVED FIVE YEARS AFTER RADIUM-INDUCED MENOPAUSE.

He operated on the patient in 1929, when she was 41, for excessive and frequent loss without uterine enlargement: 100 milligrams of radium were inserted into the uterus for 22 hours, and a cure resulted. She was quite well until this year, when she complained of discomfort and swelling in the lower abdomen. At operation a carcinoma of the left ovary was found, and panhysterectomy with removal of both appendages was done. The President showed a slide of the uterus, demonstrating a single layer of epithelium and fibrosis, and a slide of the affected ovary showing the growth. The growth had obviously no relation to the previous treatment; it was something of a shock, however, to meet with a carcinoma developing in a patient who, a few years ago, would have undergone panhysterectomy with removal of her ovaries for her first complaint of excessive loss.

Mr. J. ST. GEORGE WILSON (Liverpool) described

A CASE OF ANGULAR PREGNANCY.

Professor Munro Kerr has defined angular pregnancy as one which is implanted in one cornu of the normal uterus, which leads to preliminary enlargement of that part of the uterus before there is general hypertrophy of the main part.

Professor Munro Kerr has recently described two cases, and says he has seen four others. These cases gave rise to acute abdominal symptoms, and one case was treated as an ectopic gestation. He says that symptoms arise between the twelfth and twentieth weeks of pregnancy.

Mr. WILSON submitted that his case was one of angular pregnancy giving rise to *hyperemesis gravidarum*.

The patient, aged 26, was pregnant for the third time. Her first pregnancy was terminated for *hyperemesis gravidarum*. Her second pregnancy went to full time, but she was troubled with vomiting in the early months. Her last menstrual period was on September 1st, 1934, and she commenced vomiting on October 7th, 1934. She was admitted on October 11th, 1934, when she had albuminuria, acetonuria and a blood-pressure of 110/60.

On bimanual examination the uterus was felt retroposed and bulky, with a distinct soft bulge to the left, the main body feeling normal in shape and consistence. The size was then between eight and nine weeks. A ring pessary was placed in the vagina after replacement of the uterus, and the routine treatment of daily enemata with rectal glucose salines and injections of insulin, 10 units twice daily, commenced.

On October 25th her pulse-rate rose to 120, and she was slightly jaundiced. The urine contained a large amount of albumin and acetone with urobilin in excess. Microscopically there were many organisms and granular and hyaline casts. Mr. Wilson decided to induce abortion. In order to demonstrate the angular pregnancy, he injected lipidol into the uterus with spinal anaesthesia, and had X-ray films taken at different stages. He hoped that this would initiate abortion. As it did not do so, 24 hours later he inserted a number 10 catheter without anaesthesia. She commenced to abort the next day; the abortion was completed within 48 hours with a good deal of pain. She vomited for a day or two after abortion, then improved, and was discharged on November 15th.

Mr. Wilson invited the opinion of the Society as to (1) whether the films demonstrated angular pregnancy, and if so (2), whether it was the cause of the hyperemesis?

The PRESIDENT thought that this condition explained some cases of obscure pain in pregnancy. He considered that the X-ray photographs did not demonstrate the condition.

Professor MILES PHILLIPS (Sheffield) thought that a lop-sided uterine pregnancy was not very uncommon, and was often associated with pain. Such cases usually right themselves at 16 to 20 weeks, and then all goes well. He had seen four cases of angular pregnancy which had presented difficulties in diagnosis and management. Two had cleared up after closely simulating ectopic gestation, one had aborted after examination under anaesthesia and exploratory abdominal section for a suspected interstitial pregnancy: in the fourth case the placenta was not removable, the family doctor failed to reach it, then Mr. Phillips failed to do so: on examination under an anaesthetic he thought a fibroid was present, and removed the uterus with the retained placenta in an angular sac. Recently a similar case at the Jessop Hospital died of shock soon after admission, with the placenta retained in a thin-walled sacculation of the uterine angle—the "Tubenecken" placenta of German authors. In none of these cases was there hyperemesis.

Mr. J. E. STACEY (Sheffield) then reported three cases.

1. UNUSUAL ABDOMINAL CYST.

Mrs. T., aged 47, had four children, the youngest child was 13. She had reached the menopause about 18 months previously; she complained of gradual enlargement of the abdomen for two to three years, associated with vomiting after over-eating, and dull pain in the upper abdomen for six months. Except for one attack of jaundice three years ago, and severe constipation, her general health was good.

She had an abdominal girth of 54 inches, and a huge cystic mass filled the abdomen, which was dull to percussion in front and in the flanks. On bimanual examination the cyst filled the pelvis, pushing the cervix behind the symphysis. A diagnosis of ovarian cyst was made and laparotomy performed through an incision eight inches in length. Considerable ascites (three pints of brownish fluid) was present, and the rest of the abdomen was filled by a large thick-walled cyst apparently adherent to all the viscera but not to the parietes. Forty-six pints of brownish fluid were aspirated. This brownish fluid obviously contained cholesterol. The cyst being now collapsed, was opened through what proved to be the transverse meso-colon: in the process the transverse colon was damaged.

The House Surgeon, Mr. Patrick, a good general surgeon, now suggested the diagnosis of pancreatic cyst, and an inspection of the posterior wall of the cyst revealed what appeared to be pancreas. Marsupialization was performed and the patient, after some five weeks' drainage, left the hospital with the wound healed, and continues to be in good health now, two months later. Examination of the cyst showed the wall to contain fibrous tissue undergoing hyaline change. The papilloma removed from the floor consisted of papillae of oedematous fibrous tissue covered by low columnar epithelium occasionally re-duplicated to the pseudo-squamous type, and some of the smaller papillae were undergoing calcification. Analysis of the fluid proved the diagnosis to be correct.

This was the largest pancreatic cyst Mr. Stacey could find in an incomplete search of the literature. The cysts of the pancreas are either (1) true pancreatic cysts, or (2) pseudo-pancreatic cysts; in the former the presence of the three ferments is conclusive evidence of its origin, as in this case. They arise and spread in three marked situations, above the stomach, behind the stomach, and below the stomach, as in the case described.

Fluid.—Greenish, turbid, viscid; specific gravity 1028. Coagulable protein present, mucin present, fat present, cholesterol present, lecithin present, lipase present, trypsin present, amylopsin present; bile and hooklets nil.

2. Decidual Reaction in Adenomyoma.

Decidual reaction in an adenomyoma of the recto-vaginal septum is a rare condition. Many of the cases described as such, particularly in the ovary, are mistakes in pathological diagnosis and are really theca-lutein cysts.

Mrs. R., aged 39, a nulliparous woman married for 13 years, complained of a daily loss of blood for five weeks, which, together with pain, had necessitated her lying in bed. Prior to the continuous loss she had had 33 days' amenorrhoea; normally her periods recurred every 24 days. The pain of which she complained was stabbing in character and intermittent, like colic. There was neither fainting nor vomiting. The previous history was one of good health without dysmenorrhoea. The cervix was conical, nulliparous, slightly softened, with a small polypus protruding from the lumen; it was not blue. The uterus was bulky and mobile without pain. A tender mass, which appeared to be in the pouch of Douglas, was felt behind the uterus. A diagnosis of ectopic gestation was made and laparotomy performed.

The uterus, apparently two months pregnant, had a large irregular mass two inches, by one inch, by half an inch, growing from the lower uterine segment: to it was attached the rectum. In the process of removing the mass, which was likely to involve difficulty at the confinement, Mr. Stacey was under the impression that it was either a carcinoma of the rectum or an adenomyoma of the recto-vaginal septum: the latter diagnosis was proved by section to be correct.

In the course of removal the cavity of the uterus was opened, and as most of the cervix had been removed at the same time and yet a considerable amount of tissue had been left behind, it was decided that hysterectomy with double salpingo-oöphorectomy was the right line of treatment, and this was performed. There were four or five fibroids, subserous and intramural, one of which was the size of a walnut and invaded the uterine cavity. A plaque of tissue was still left adherent to the rectum. The section shows a typical adenomyoma of the recto-vaginal septum with decidual reaction, and the uterus contained a foetus measuring two and a half cubic centimetres in length.

3. Radium in Epithelioma of Vulva.

Mr. Stacey recorded five failures of treatment of epithelioma of the vulva by radium, subsequently treated by diathermy excision.

(*a*) *Mrs. A.* was aged 60; she had had seven children, the youngest of whom was aged 20; she had reached the menopause at 50, and complained of ulceration of the vulva for 20 years. There was a considerable leucoplakic condition of the vulva, with an ulcer half an inch in diameter in the left *labium minus*. The ulcer on section was an epithelioma, and some enlargement of glands was present in each groin. Radium (25 needles containing three milligrammes) was applied for three to four days—5,400 to 7,000 milligramme-hours. It was also applied all round the ulcer and both inguinal regions. Much relief was obtained for 12 months, though the ulcer never quite healed, and severe pain and glandular increase occurred for a further 12 months, in spite of deep X-ray therapy. The ulcer was now one inch in diameter, and two years after the radium had been applied excision of the vulva with both groups of inguinal glands was performed. An examination of the sections showed epithelioma with involvement of glands to be present.

The other four cases were much more rapid in their recurrence.

(*b*) *Mrs. R.* was aged 80; the youngest of her five children was 42 years old, and she had had the menopause 42 years ago; she had noticed an ulcer of the vulva for five years, and on account of the pain and the fact that the ulcer was a malignant papilloma of low-grade malignancy, radium was applied, but within three months the pain and discharge from the ulcer had become so much worse that radical excision by diathermy was performed, and there were two secondary patches shown by section to be radium burns which were not malignant.

The old lady unfortunately succumbed to her operation on the eleventh day.

(*c*) *Mrs. M.* was aged 58; the youngest of her seven children was 13 years, and she had reached the menopause 10 years ago; she complained of pain with an ulcer of the urethra for about two months. The urethral orifice was invaded by a friable granular mass, easily bleeding, half an inch in diameter with enlarged glands in the left groin. Section showed an epithelioma, and radium was applied. Three months later the ulcerated area had extended with infiltration of the left labium to a diameter of one inch and marked involvement of the glands of both sides. The pain was intense and radical excision by the diathermy knife was performed.

(*d*) *Mrs. B.* was aged 70; the youngest of her five children was aged 22; she had reached the menopause at 50, and complained of ulceration of the vulva for about 12 months. Radium (5,400 milligramme-hours) was applied to what on section was proved to be an epithelioma, and relief was obtained for three months. Severe pain occurred during the next three months, which became so excessive as to necessitate excision by diathermy. The sections now showed a low-grade epithelioma with a radium burn.

(*e*) *Mrs. S.* was aged 36, with one child aged 12; she complained of vulval irritation for 12 months. Section showed an epithelioma of the clitoris with glands involved by malignant growth. Radium was applied with relief for three months, when intense pain necessitated a radical excision. Evidence of malignancy with a burn was still present.

Mr. STACEY had been impressed for some considerable time by the inefficiency of radium for the treatment of epithelioma of the vulva. Where the ulcer fails to heal, extension is rapid and radium burns cause such severe pain that local excision is demanded in a very short time.

Two years ago at Leeds an interesting discussion on the subject arose from a case in which one brother advocated excision, stating that no patient survived 12 months after radium, and the other advocated radium stating that none survived for 12 months after excision. Possibly a judicious combination of both, with the addition of deep X-rays, would appear to be the right procedure, but Mr. Stacey sought the advice of other members of this Society.

The PRESIDENT asked if there had been any glycosuria in the first case. Referring to the second case, he asked what the condition of the ovaries had been. He considered that the condition of adenomyoma of the recto-genital space was common in association with ovarian endometrioma. He regarded the radium treatment of epithelioma vulvae as not only painful but also useless.

Mr. WILSON asked whether both ovaries were removed in the second case. He thought that the dosage of radium had been too heavy in the cases of vulval carcinoma, and that the glands should always be removed surgically.

Professor W. GOUGH (Leeds) said that he had seen three cases of endometrioma of the recto-genital space this year. He thought that Mr. Stacey's case was cervico-rectal. He was in the habit of treating carcinoma vulvae successfully with radium, which was better and safer than radical operation. He had no faith whatever in deep X-ray therapy for malignant disease.

Mr. A. A. GEMMELL (Liverpool) agreed with Mr. Wilson that the dosage of radium in the cases of epithelioma vulvae had been too heavy.

Dr. J. W. BURNS (Liverpool) asked about the healing of inguinal wounds in these cases.

Dr. W. D. GALLOWAY (Holmfirth) mentioned a case in which he had excised the vulva and inguinal glands for epitheloma of the vulva: there was subsequent sepsis of the wound, and the patient died six weeks later, probably from pulmonary embolism. Sepsis of the inguinal wounds was a great difficulty in these cases.

Mr. STACEY, in reply, said that he was sure there was no glycosuria in the first case: in the second case he excised the ovaries; both were devoid of tar cysts and healthy. He said that inguinal wounds healed well if the excision was done with the diathermy knife; they were sewn up completely except for a drain over the symphysis. He minimized tension by the use of lateral cuts. He agreed with Mr. Wilson that the inguinal glands should be removed surgically.

Dr. W. J. RAWLINGS (Manchester) read a paper on

NEMBUTAL IN CHILDBIRTH, WITH A REVIEW OF 241 CASES.

This paper is a review of the administration of nembutal in St. Mary's Hospital during the 12 months February 1933 to February 1934. The number of cases in the series was 241, i.e. about one-tenth of the total maternity admissions. This apparent selection of cases was governed solely by the reaction of the patient to labour: if she was restless, having severe pain, or looked like having a long labour in which a sedative would be useful to conserve strength, nembutal was administered; if, however, labour was so far advanced or was proceeding comfortably without distressing the mother, she carried on naturally or had a terminal anaesthetic. Unfortunately, case-sheets were not written up with a view to future discussion, and several points on which I would now like to have information were omitted.

The administration was altered during the period from a strict routine to a method in which judgment in dosage was used rather than a fixed rule. Thus the initial method was three grains of nembutal and 20 grains of chloral hydrate, with repeated doses similar to the method of O'Sullivan and Craner. I did not like this method, the uterine contractions appearing to diminish in intensity, and certainly in frequency; if commenced early the patient tended to fall out of labour. There were 10 cases in this group.

When to commence administration. I fell back on my experience of Gwathmey's rectal ether, which I still consider very good. The patient must be in regular labour, and have regular uterine contractions at intervals of not more than three minutes, each contraction lasting 30 to 40 seconds. If this period of labour is worrying the mother, nembutal is commenced irrespective of parity and of the dilatation of the cervix.

A rule was gradually evolved that an initial dose of three grains of

nembutal (two capsules) should be given, followed by an hourly review of the case. At the end of the first hour nembutal is again given in doses of three grains, one and a half grains, or none, depending on the restlessness of the patient, her response to questions, her response to uterine contractions, but most of all her condition between contractions. If the patient is well under she dozes to sleep between contractions, will respond to irritating stimuli, and will wake up to answer questions, but not intelligently. If she is not so well under, dosage is given as stated, the patient usually being persuaded to swallow the capsules without any difficulty.

Of cases requiring a repeated dose of three grains, there were 20 (approximately eight per cent), 12 of these being at the end of the first hour: that is practically equivalent to the method advocated by some writers, i.e. an initial dose of six grains. Six cases had a repeat dose of three grains after longer intervals, one had it interspersed among doses of one and a half grains, and one case of especial interest, her second labour, aged 33 years, received dosage as follows: At two hours three grains, at four hours three grains, at six hours three grains, at eight hours one and a half grains: natural delivery of a baby weighing seven pounds 14 ounces occurred at 14½ hours. This patient, in spite of 10½ grains in six hours, was restless throughout but had complete amnesia. Naturally, the amounts given vary considerably, and I propose dividing the cases into groups of single doses, two, three, four, five, and six doses.

In the first group, with a single initial dose of three grains, there are 94 cases, which is a larger number than was anticipated in starting the report, and one of the fallacies of dosage and administration lies in this series. Many of these patients were primiparae, normal in obstetrical respects, who carried on quietly until well into the second stage; when becoming restless they were given nembutal, the patient being delivered before more was required.

These cases were interesting in that many quietened or became more amenable to suggestions and instructions: most certainly had an incomplete amnesia of the second stage but the effect as regards nursing staff was often not so helpful. In all cases the patient immediately after the third stage dropped off into a deep sleep. From these the conclusion arises that nembutal to be given in comparatively small doses requires earlier and prolonged administration.

The two-dose group numbered 69, nearly one-third of the total, of which 38 had three grains with one and a half grains at the end of one hour; 16 at the end of the second hour, the remainder at longer intervals. Eight cases of this group were included in the double three series, of which number 60 were given three grains at intervals of eight hours, i.e. at 41 and 49 hours, with normal delivery at 60 hours, the good effect in quietness and amnesia is interesting to note.

The three-dose group. Thirty-nine cases: the second dose of one and a half grains was given in one hour to half of the patients, the remainder mostly received it in the second hour: the third dose was administered in the majority after an interval of two to three hours.

The four-dose group of 17 cases practically followed the previous group in time spacing with an average interval of three to four hours between the third and fourth doses. Of this group No. 147 received at 25 hours three grains, at 26 hours one and a half grains, at 29 hours one and a half grains, at 34 hours one and a half grains: normal delivery occurred at 36 hours. No. 281 received at eight hours three grains, with one a half grains at 10, 12 and 16 hours: normal delivery occurred at 22 hours. No. 1,522 is interesting because of the rapidly repeated dosage and effect, thus: at 14 hours three grains, with one and a half grains at 15½, 16½ and 18 hours; the effect was very good: the patient was drowsy and stuporose, but the uterus contracted well and the presenting part advanced till 29 hours when the patient roused and was delivered normally at 30 hours of a living baby weighing eight pounds. The pelvic measurements were: I.S. 10¼ inches, I.C. 10¾ inches, D.C. 4¼ inches. No. 2,498 was admitted in labour with a transverse lie. External cephalic version was done under anaesthesia, followed by three grains at nine hours, and at 10, 11 and 12 hours one and a half grains. She previously had 10 children and required quietening for natural delivery at 14 hours. In this case, on reconsideration, I think larger doses could have been used in the early part of labour with advantage.

The five-dose group. Nine cases. Out of the chaos of time-dosage tables I have been unable to evolve a routine: the intervals vary considerably; thus one patient received nine grains in eight hours, while another had nine grains in 26 hours. No. 1,528 was a primipara at term with an occipito-posterior position. At nine hours she received three grains, at 11 hours one and a half grains, at 12 hours one and a half grains, at 17 hours one and a half grains, and at 22 hours three grains. There was good analgesia: she was working with contractions, and dozing between: at 26 hours there was no advance, though the caput had showed for three hours: under a general anaesthetic manual rotation was done from transverse to occipito-anterior. She was then left alone till 30 hours, when a baby weighing seven pounds, which was rather asphyxiated but revived comfortably, was born normally. In this case, taking nine hours as zero, the time-table is: at zero three grains, at two hours one and a half grains, at three hours one and a half grains, at eight and 13 hours one and a half grains, at 17 hours general anaesthetic, at 21 hours normal delivery.

No. 748 was a primipara aged 34 years. At 35 hours three grains were given, at 40 hours one and a half grains, at 44 hours three grains, at 50 hours one and a half grains, at 61 hours one and a half grains, at 68 hours the head was rotated manually and a living baby weighing eight and a half pounds was extracted with the forceps. (Note the second dose of three grains.)

No. 1,389. A primipara, with an occipito-posterior position, was admitted for long first stage of labour, 60 hours. On admission a quarter of a grain of morphia was given and was followed by a short sleep, then three grains of nembutal were given at 67 hours, at 70 hours three grains, at 72 hours one and a half grains, at 74 hours one and a half grains, at 77 hours one and a half grains, and at 83 hours a living baby weighing eight pounds two ounces was born normally followed by a restful sleep of 12 hours.

No. 2,225 was a failed-trial-labour primipara. At seven hours she

received three grains; at nine hours, 10½ hours, 13 hours, and 17 hours one and a half grains: the effect was good at first, but later she became restless from under-dosage, as it was desired that the patient should have full use of her secondary forces. At 24 hours, when the cervix had been fully dilated for 12 hours, the membranes ruptured and the vertex was impacted just in the brim. Caesarean section was done under ether anaesthesia: a living baby weighing seven pounds twelve ounces was delivered: there were no after-effects.

The six-dose group. There were only three cases, but each is worthy of consideration.

No. 827. This patient was a primipara, with a diagonal conjugate diameter of 4¼ inches; she received at 11 hours three grains, with one and a half grains at each of 13, 15, 18, 21 and 25 hours. Normal delivery of a live baby, weighing six pounds twelve ounces occurred at 27 hours; here a total of 10½ grains was given with almost regular three-hourly spacing.

No. 1,196. Perhaps this is the best case of all. The patient was a primipara with a small round pelvis (diagonal conjugate 4¼ inches). At 17 hours she received three grains, half an hour later she vomited; at 18 hours she was not under the influence of the drug and received a second dose of three grains. At 20, 23, 27 and 32 hours she received one and a half grains. Normal delivery of a baby weighing six pounds three ounces occurred at 34 hours. As regards amnesia, I saw this case at 11 p.m. and ordered nembutal: labour continued with the patient well under, and she was delivered at 4 p.m. the following day; she then slept until lunch time on the next day: when she awoke she was feeling refreshed and well: the last thing she remembered was "when that fellow came at night and ordered the pills." In this case the total dosage was 12 grains over a period of 15 hours.

No. 1,322. This was a case which caused me to think deeply and carefully watch subsequent cases. The patient was a primipara aged 18 years, the position a left occipito-posterior; she was in labour. At 20 hours three grains, 21½ hours one and a half grains, 24 hours one and a half grains were given. The patient now had good strong contractions: she was pushing well and analgesic though restless. At 26 hours there was slow advance with contractions: the os was three-quarters dilated with a thick anterior lip and the sagittal suture was in the transverse diameter of the pelvis. Under anaesthesia manual rotation to the left occipito-anterior position was done. At 28 hours she was very restless and noisy; one and a half grains of nembutal were given: there was little effect and the dose was repeated at 29 hours: again at 32 hours one and a half grains were given. When nicely under and working well since restarting nembutal, at 35 hours the patient became apnoeic and cyanotic though the pulse-rate was regular at 90, with good volume and tension, the pupils not strongly contracted. Carbon-dioxide and oxygen were given shortly after, but she became apnoeic again and required artificial respiration. At 36 hours carbon-dioxide was given as the breathing was unsatisfactory, an anaesthetic was given and a low forceps delivery of a living baby weighing eight pounds seven ounces, which cried immediately, was carried out. Half an hour later the placenta was expelled with a fair loss: pituitrin and femergin were given. At 37 hours

respirations were shallow and the colour was bluish though the pulse was good: carbon-dioxide was given. At 37½ hours she was conscious to painful (pin) stimuli. At 38 hours there was collapse of the pulse and respiration: artificial respiration was done and stimulants and intravenous glucose were administered: there was a ready response. At 42 hours she had improved. At 56 hours she was conscious and talking; the condition was quite good, as though there had been no previous trouble: the puerperium was normal: the total dosage was 10½ grains in 12 hours.

Following on this rather disquieting apnoeic case, I watched cases of albuminuric toxaemia, and since then have treated 20 definite cases of albuminuria and one of eclampsia. In none was there any untoward effect: the average dosage was four and a half grains, i.e. three and one and a half grains. One case had nine grains in 10 hours, and another nine grains in 13 hours.

Six cases in which the forceps had been applied unsuccessfully before admission were treated: this number is small as the results were not encouraging. The patients after strenuous efforts and one or more anaesthetics before admission were usually not good subjects. Sister and I agreed that nembutal is useful, but morphia, or morphia and scopolamine, gives better results.

There were only two cardiac cases. One of these was a primipara with mitral stenosis and 2,648,000 red cells per cubic millimetre of blood: the case was unusual in that progress was slow for a cardiac case, labour lasting 24 hours: and she required an analgesic, having seven and a half grains with good effect.

Cases terminating in forceps delivery totalled 46, i.e. 18 per cent: in this connexion one must remember that analgesia was required because labour was long and painful and that most of the cases were occipito-posterior and did not rotate. The large incidence of occipito-posterior cases in Lancashire, and the frequent failure to rotate always interested me whilst at St. Mary's, though I am not discussing it now.

Effect on baby. In my opinion nembutal does not adversely affect the baby, the foetal heart-rate and rhythm being maintained as in non-analgesic cases. My confidence is best illustrated by a case (No. 1,483) in which the foetal heart-rate was 200 and irregular in a primipara at the onset of labour; this was a rather disquieting state of affairs. Nembutal was administered, in all nine grains in 22 hours, with a good effect on the mother: the foetal heart-rate remained exactly the same throughout the whole labour: the baby was born spontaneously and cried lustily.

Sixteen cases of stillbirth were recorded: nine were inevitable, as the foetal heart was not heard on admission. The case histories of the remaining seven are:—

No. 1,910. The patient was a primipara. At 16 hours she received three grains with good effect; at 19 hours the caput was visible; at 19½ hours the foetal heart was inaudible; episiotomy was done, followed by a low forceps delivery. The child was stillborn.

No. 1,935. The patient was a primipara; the presentation a right occipito-posterior. At 18 hours she received three grains, at 19 hours one and a half grains, at 36 hours low forceps delivery was undertaken and a stillborn baby weighing six pounds eight ounces was extracted.

No. 2,131. This patient was in her second labour. At 16 hours she received three grains, at 18 hours one and a half grains, at 22 hours normal delivery occurred. The baby was stillborn and weighed five pounds two ounces.

No. 2,171. The patient had previously had 10 children; the urine contained a heavy cloud of albumin. The presentation was a breech with extended legs. The total dosage was four and a half grains. The baby, weighing nine pounds four ounces, was extracted stillborn.

No. 2,365. The patient was a primipara. She received at 32 hours three grains, at 36 hours a stillborn baby weighing five pounds was born normally.

No. 2,514. The patient had previously had two children, the first was stillborn and the second was macerated. Bougie induction was done. At 11 hours she received three grains, at 12 hours a stillborn baby weighing seven pounds was born normally.

No. 2,142. This was a case of shoulder presentation: an easy internal podalic version was done: she received one dose of one and a half grains. Normal delivery of a stillborn baby weighing five pounds four ounces followed.

Five of the above cases were complicated by malpresentation or medicinal induction.

Cases of foetal distress and asphyxia, five:—

No. 216. Labour began at the thirty-eighth week; the pelvis was small. At eight hours she received three grains, at 10 hours one and a half grains, at 12 hours the cervix was fully dilated; a low forceps delivery was undertaken and the child was stillborn.

No. 912. The position was a right occipito-posterior. Labour lasted four days, manual rotation and forceps extraction were carried out, and the baby was living.

No. 1,528. A primipara; received five doses in 21 hours with good effect. The baby was asphyxiated, but responded to treatment.

No. 1,974. The patient was a primipara; at 10 hours she received three grains, at 11 hours one and a half grains without effect. At 15 hours low forceps delivery was undertaken; the baby had white asphyxia: it responded to treatment.

No. 1,038. The patient was a primipara, aged 44 years: at two hours she received three grains; she became very drowsy and at four and a half hours normal delivery of a baby weighing eight pounds two ounces occurred: there was slight asphyxia. In this case the mother was very drowsy, but the foetal heart remained good, and perhaps the rapid labour was the more important factor.

Results. In exact figures the results are not easy to determine. In some cases I have relied on ward reports where "good effect" may merely mean a quiet restful labour for the nurse in charge. However, two points require consideration. (1) Restlessness and relief of pain, and (2) amnesia. Nine cases, i.e. 36. per cent, were "bad"—i.e. there was no effect in either direction: several of these were single doses administered too late to be effective, though all slept well post-partum. Thirteen, i.e. 52. per cent, were very good: there was absolute quietness and amnesia. The remainder varied in restfulness though all were subdued: in most amnesia was complete though some had hazy recollections with intermittent patches of light: the vast majority, roughly 80 per cent, might be classed as good results.

Conclusion to be drawn.

1. Nembutal orally as an analgesic and amnesic is a useful adjunct to midwifery.

2. It is best administered in small doses as required. Patients react differently, and I do not advocate large initial doses.

3. The time to commence administration is when the patient is in regular labour with contractions every three to four minutes lasting 30 to 40 seconds. I do not worry about the dilatation of the cervix.

4. The case should be reviewed at approximately hourly intervals for further administration of nembutal. This is the objection in private practice where the general practitioner desires a sedative which will have a safe effect for several hours not requiring his attendance.

Dr. R. NEWTON (Manchester) said that the sisters at St. Mary's did not like a routine for nembutal: they much preferred individualized dosage.

Mr. A. A. GEMMEL (Liverpool) said that nembutal had been given up at Liverpool after experience with only 12 cases. The forceps rate had been very high, and there had been three unexplained stillbirths.

Dr. RAWLINGS, in reply, said that he changed from a routine to an inidividualized method of administration because of the restlessness of the patients. He believed in pushing the drug till the patient was "knocked out": this abolished restlessness. Chloroform after nembutal was quite safe.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY.

A meeting of the North of England Obstetrical and Gynaecological Society was held at Manchester on Friday, December 14th, 1934, with the President, Professor Daniel Dougal, in the chair.

The PRESIDENT read an address arranged in the form of a Platonic dialogue. Unfortunately for the readers of this journal the address was entitled "Private and Confidential."